DECOMPOSITION OF ACYLARYLNITROSAMINES AND RELATED REACTIONS

by

J. Rowland Mitchell, B.Sc.

Thesis presented for the degree of
Doctor of Philosophy.

University of Edinburgh September, 1971

I declare that this thesis is my own composition, that the work of which it is a record has been carried out by myself, and that it has not been submitted in any previous application for a Higher Degree.

The thesis describes results of research carried out in the Department of Chemistry, University of St. Andrews and the Department of Chemistry, University of Edinburgh, under the supervision of Professor J.I.G. Cadogan since the 1st October, 1968 the date of my admission as a research student.

ABSTRACT

The reactions of N-nitrosoacetanilide with furan and 2,5-dimethylfuran have been investigated. Competition reactions involving a variety of sources of phenyl radicals and benzyne/benzynoid intermediates showed that the rate ratio $K^{furan}_{benzene}$ was highest in those reactions involving the intermediacy of the benzenediazonium cation. This observation led to a proposed mechanism for the decomposition of N-nitrosoacetanilide in furan, which involves a redox reaction between the benzenediazonium cation and the 2-phenyl-2,5-dihydrofurfuryl radical. The puzzling lack of benzyne adduct in this reaction was resolved, when a high temperature reaction gave the adduct 1,4-dihydro-1,4-epoxynaphthalene in low yield, a fast redox reaction apparently takes precedence at lower temperatures.

A detailed investigation of substituent effects, temperature effects, and the effect of water on the decomposition of N-nitrosoacetanilide in 2,5-dimethylfuran was carried out. The formation of products derived from phenylation of the methyl groups on the furan nucleus was found to be particular to 2,5-dimethylfuran, and a mechanism for the reaction is proposed. The mechanism is thought to proceed through the formation of a π-complex between 2,5-dimethylfuran and the benzenediazonium cation, thereby increasing the acidity of the methyl protons. The basicity of acetate ions, under anhydrous conditions, is considered high enough to abstract a proton from one of the methyl groups, and the attack of the resulting intermediate upon the benzenediazonium cation

leads directly to 2-benzyl-5-methylfuran. A mechanism for the formation of substituted pyrazoles, which were isolated from reaction mixtures during the course of this investigation, is also proposed.

Knowledge of the fact that water suppresses the formation of benzyne adducts in the decomposition of N-nitrosoacetanilide has led to the development of two new syntheses of arynes. The effect of water was quantitised in the case of the decomposition of N-nitrosoacetanilide in the presence of 2,3,4,5-tetraphenylcyclopentadienone, and was shown to have a similar effect on the yield of benzyne from the decomposition of benzenediazonium fluoroborate in the presence of acetic acid and potassium acetate. The reaction of pentyl nitrite and aniline, which has found use as a source of phenyl radicals for some time, was carried out in the presence of acetic anhydride, and 2,3,4,5-tetraphenylcyclopentadienone. The benzyne adduct, 1,2,3,4-tetraphenylnaphthalene was isolated in 32% yield from this reaction. Further investigation of this reaction led to the assumption that acetic anhydride was reacting with pentyl nitrite to form transient acetyl nitrite, which was nitrosating the acetanilide formed in the reaction mixture, giving N-nitrosoacetanilide. From this assumption, the new reagent 4-chlorobenzoyl nitrite was developed to perform the in situ nitrosation of acetanilide. 1,2,3,4-Tetraphenylnaphthalene was isolated in 70% yield when the reaction of 4-chlorobenzyl nitrite and acetanilide was conducted in the presence of 2,3,4,5-

tetraphenylcyclopentadienone.

A preliminary report on the formation of benzyne from the reaction of organic nitrites with aniline, and its derivatives has been published (J.I.G. Cadogan, J.R. Mitchell and J.T. Sharp, J. Chem. Soc. D, 1971, 1).

ACKNOWLEDGEMENTS

I should like to express my thanks to Professor, J.I.G. Cadogan for suggesting the topic of research, and to Professor Cadogan and Dr. J. T. Sharp for their continued advice and encouragement during the period in which the work was carried out.

In addition, I wish to record my thanks to many members of the teaching, technical and secretarial staffs in the Department of Chemistry of both the University of St. Andrews and the University of Edinburgh for their assistance at various times.

Finally, I should like to thank the Science Research Council for the award of a Research Studentship for the period during which the work was carried out.

CONTENTS

I N T R O D U C T I O N

PREAMBLE.

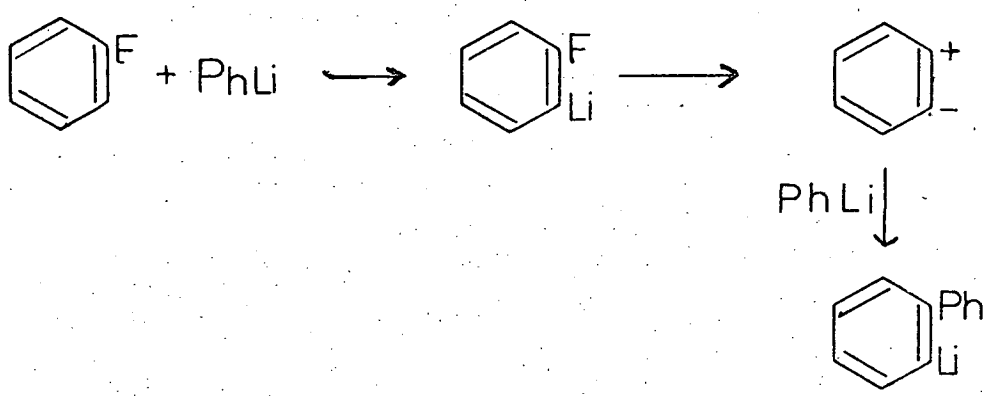
Acylarylnitrosamines have been known for nearly one hundred years, and have found use as a synthetic route to biaryls for nearly forty years. Despite this fact, the mechanism of the decomposition of acylarylnitrosamines had eluded workers until in the past few years, a seemingly satisfactory mechanism for the route to biaryls has been postulated. At the same time, however, the overall mechanism for the decomposition has been complicated by evidence that arynes are being produced as intermediates in the decomposition.

The two intermediates responsible for the reaction products - radicals and arynes - had been postulated for some time before their general acceptance as recognised reactive intermediates, their childhood being prolonged by the inflexibility of some of the workers of the time to the wind of scientific thought.

In three short reviews, the background to each of these three subjects - arynes, radicals and acylarylnitrosamines - is covered, as a prerequisite to the work discussed in the latter part of this text.

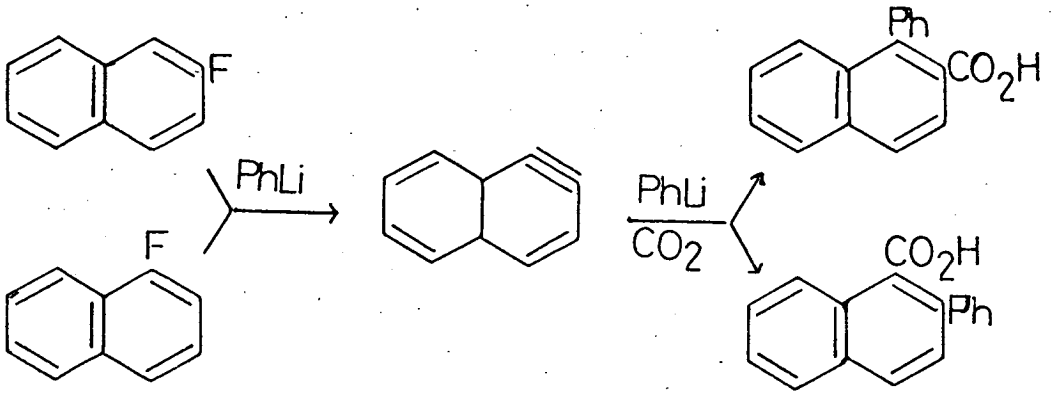
1 ARYNES.

Although reactions involving arynes had been in use for nearly eighty years, it was not until 1942 that Wittig[1], investigating the reaction of phenyl-lithium with fluorobenzene[2], successfully rationalised the mechanism. Wittig showed that the extremely rapid production of biphenyl in this reaction was due to the formation of the primary product 2-biphenylyl-lithium which subsequently decomposed to give biphenyl. Wittig suggested the participation of the permanently charged 1,2 - dehydrobenzene intermediate (scheme 1).

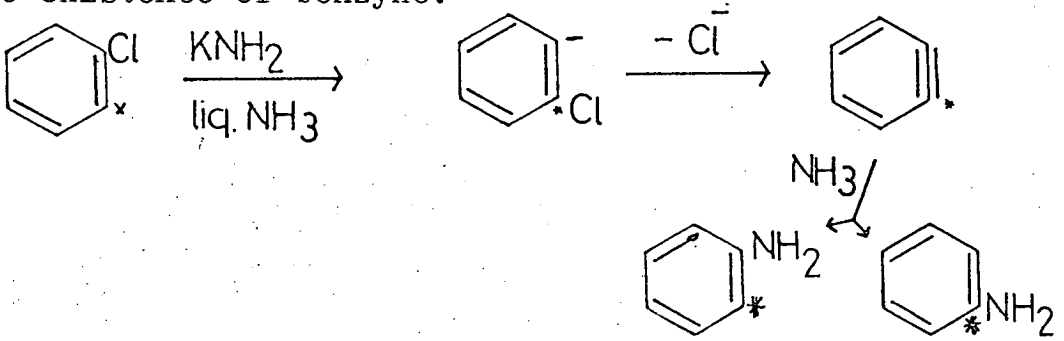


Scheme I

This scheme used the unusually high acidity of the o-hydrogens of fluorobenzene to explain the high rate of reaction. Wittig's formulation of benzene, however, was to be modified by Huisgen and Rist [3,4], who examined the products of the reaction of 1- and 2-fluoronapthalenes with phenyl-lithium followed by reaction with carbon dioxide. They found the same ratios of 1-phenylnaphthalene – 2 — carboxylic acid and 2-phenylnaphthalene – 1-carboxylic acid in the products from each of the starting compounds, and pointed out that this was incompatible with Wittig's permanently charged species.

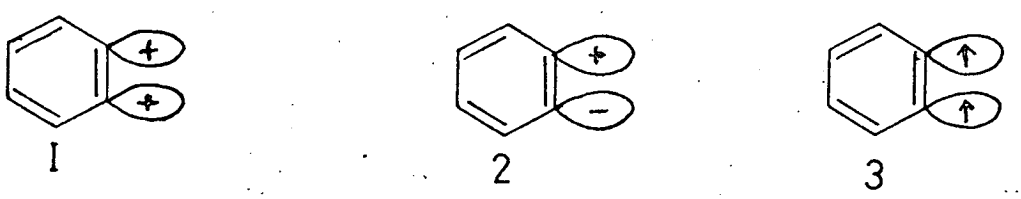


Roberts[5], in an elegant experiment, examined the reaction of C^{14} labelled chlorobenzene, and potassamide in liquid ammonia. He obtained equal amounts of two different isotopically labelled anilines thus proving, by the cine substitution, the existence of benzyne.



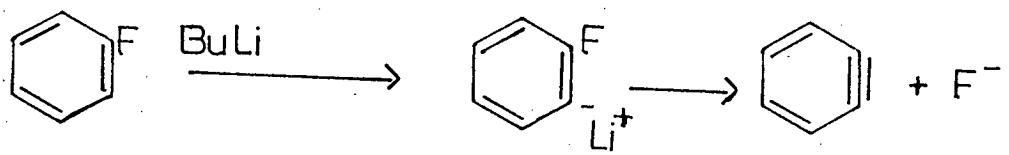
The existence of benzyne in the gas phase had been demonstrated by time resolved mass spectroscopy[6] and by absorption spectroscopy[6b, 7].

The structure of benzyne was assumed[17] to be one of the two singlet structures - symmetrical, 1 and antisymmetrical, 2 - or the triplet structre, 3.

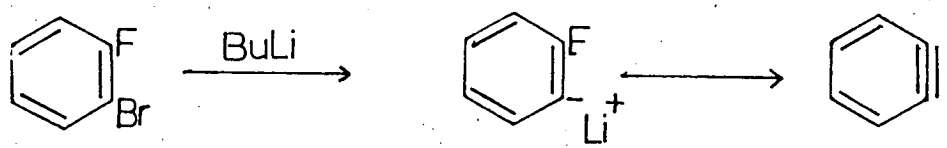


The triplet form was discounted early in the investigation of the intermediate[8], and no supporting evidence has been found since that time which has suggested its existence in solution. Of the two remaining structures, 1 and 2, recent work has confirmed the symmetrical singlet structure[9,10].

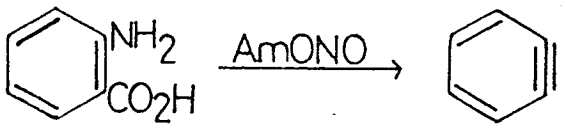
Originally, the only known sources of benzyne were from the decomposition of o-anionised benzene derivatives, which were usually prepared by the action of organometallic bases on the benzene derivative. This is exemplified in the metallation of fluorobenzene using butyl-lithium[11] and by the



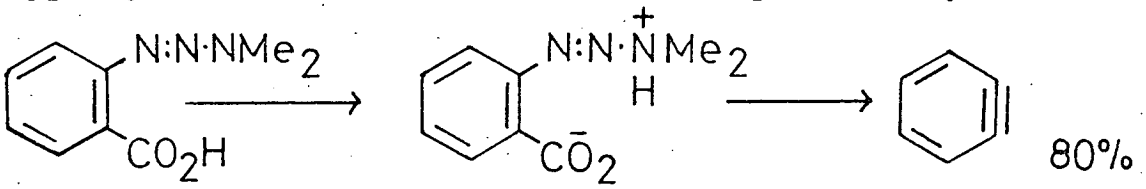
action of butyl-lithium on o-bromofluorobenzene[12].



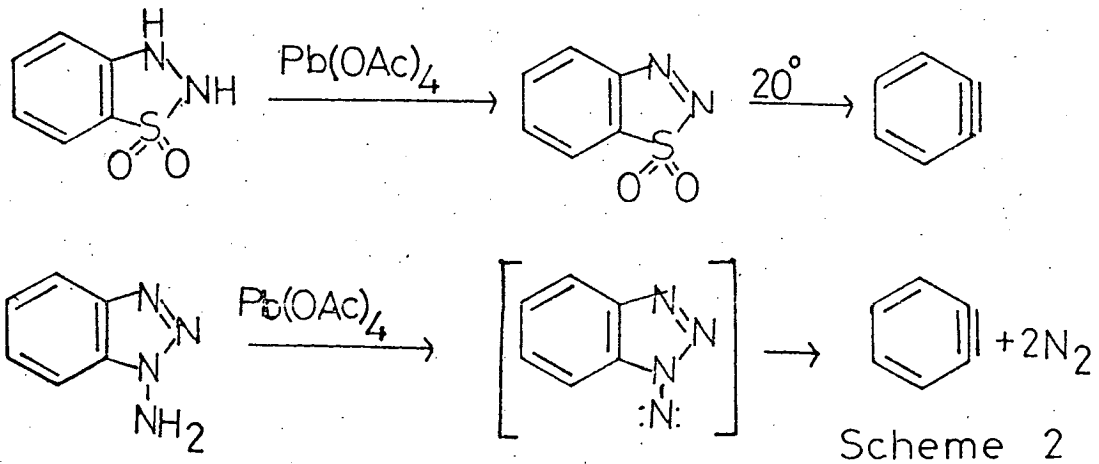
The great disadvantage of the use of strong bases to generate arynes is that the bases themselves are usually good nucleophiles, so that products obtained are those of addition of the base to the aryne. The breakthrough in the synthesis of arynes came with the dispensing of the need for strong base. Benzenediazonium-2-carboxylate was found to decompose with the evolution of carbon dioxide and nitrogen[13-16] to give benzyne which was captured in yeilds of approximately 30% by trapping with anthracene[15]. The explosive nature of benzenediazonium-2-carboxylate made it rather unattractive, but a modification of the reaction by Friedmann[18], utilising the in situ diazotisation of anthranilic acid with pentyl nitrite produced high yields of benzyne under extremely mild conditions.



This discovery was quickly followed by related schemes involving elimination of small molecules from o-disubstituted or fused heterocyclic derivatives. Thus 1-(2 carboxyphenyl) triazens were found to decompose to arynes[19],



and oxidation of heterocyclic systems with lead tetraacetate has been found to generate benzyne in good yields. For example the oxidation of 1,2,3-benzothiadiazolin-1, 1-dioxide[20] to 1,2,3-benzothiadiazole-1, 1-dioxide which readily decomposes to benzyne; and the oxidation of 1-aminobenzotriazole[21] which again gives benzyne (scheme 2).

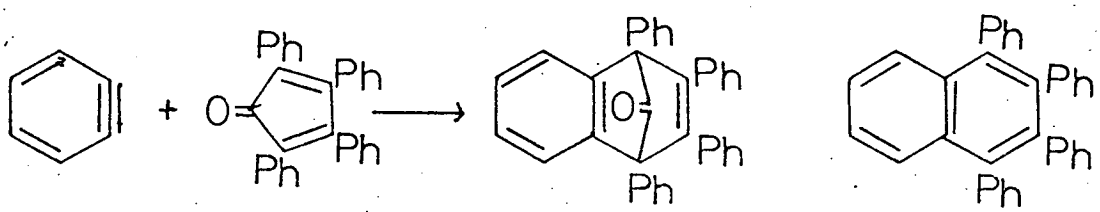


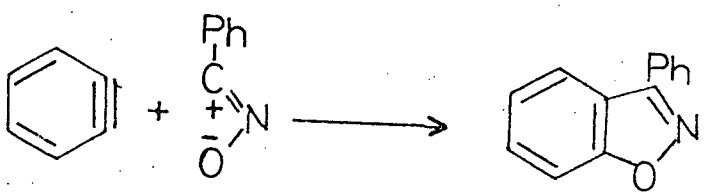
Scheme 2

The recent discovery that not only o - t - butyl - N - nitrosoacetanilide[24] but also N-nitrosoacetanilide itself gave benzyne adducts when decomposed in the presence of aryne traps, has opened a new field in the simple production of arynes in solution.

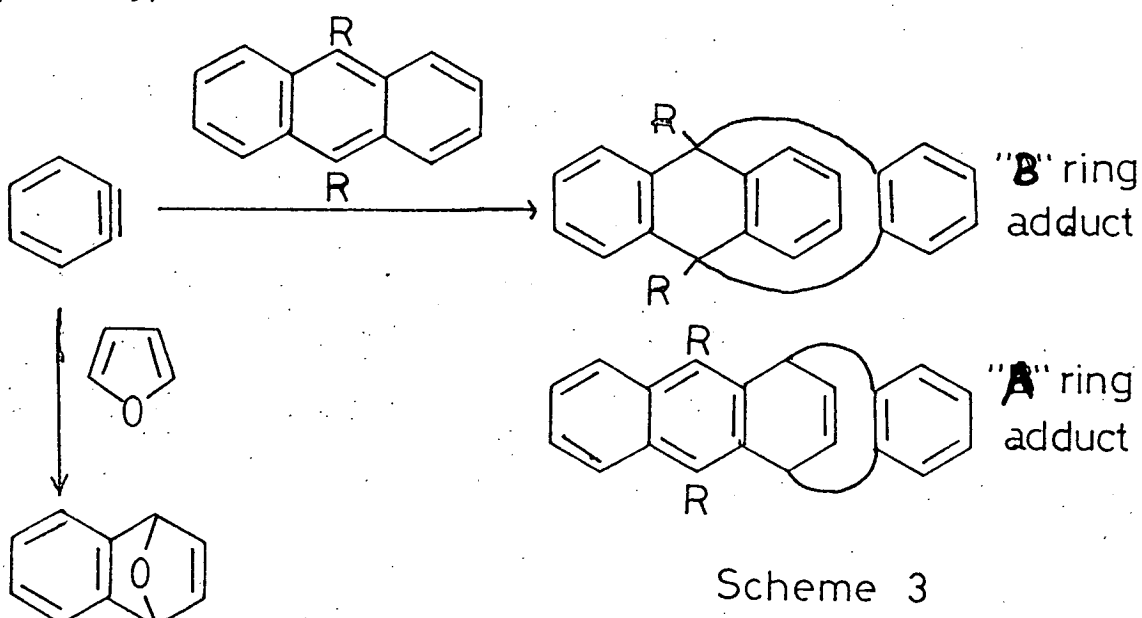
The question of aryne participation in the decomposition of acylarylnitrosamines will be discussed later in this text.

In the presence of dienes, arynes behave similarly to highly reactive acetylenes, performing Diels-Alder cycloadditions, and in the presence of 1,3-dipoles, 1,3-dipolar cycloadditions. Thus: with 2,3,4,5-tetraphenylcyclopentadienone (tetracyclone), benzyne gives 1,2,3,4-tetraphenyl-





naphthalene[21], and with benzonitrile oxide[25], 3-phenylbenzisoxazole. The Diels Alder reaction of arynes, and in particular the reaction with tetracyclone, is the most commonly employed chemical means used to detect the presence of arynes in a reaction mixture. Other regularly employed diene traps are anthracenes[13,18] and furan[26] giving triptycenes and 1,4-dihydronaphthalene - 1,4-endoxide respectively (scheme3).



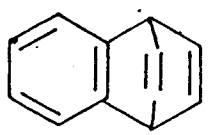
Scheme 3

The reaction of benzyne with anthracene was originally thought to give only triptycene, however a thorough investigation of the reaction by Klanderman[27] showed that, as well as the normal "B" ring product of triptycene, there was also a small quantity of the "A" ring adduct 5,12-dihydro-5,12-ethenonaphthacene (scheme3). He found that the proportion of "A" ring adduct could be increased by having electron-attracting substituents at positions 9 and 10 or electron-repelling substituent at positions 1 and 4 on the anthracene. Klanderman and Criswell[28,29] measured the ratio of "A" ring to "B" ring adducts for a variety of substituted anthracenes and found it to be independent of the source of benzyne. This reaction has been used as a test for the presence of benzyne intermediates in solution.

In the absence of any other substrate, benzene itself can act as a diene, reacting with benzyne[13,14] to form benzo-bicyclo - (2,2,2) - octatriene (9%), 4, benzocyclo-octa-tetraene (2%), 5, and biphenyl.

Friedman[30] showed that the high yield of biphenyl and benzocyclo-octatetraene was due to silver ion contamination in Miller and Stiles' benzyne precursor, which was stabilising the benzyne. He showed that in the absence of silver ions, the major product was benzobicyclo-(2,2,2,)-octatriene, (17%).

Arynes react with some olefins to give 1,2-cycloadducts, exemplified by the reaction of benzyne and trans-cyclo-octene[32].



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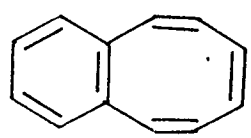

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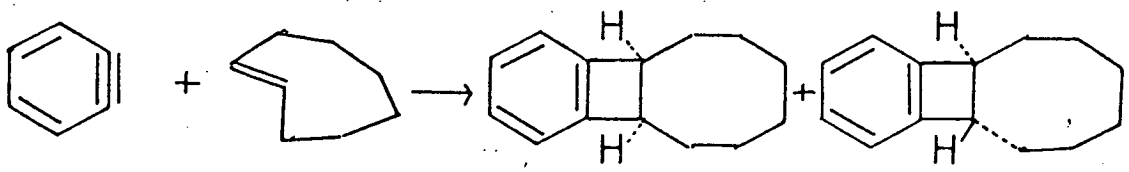
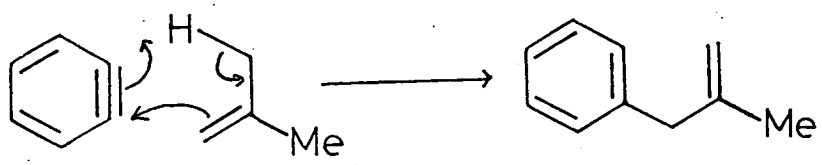
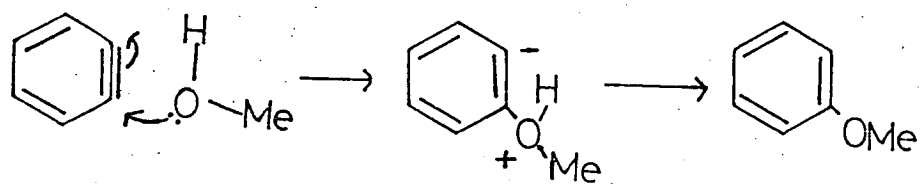


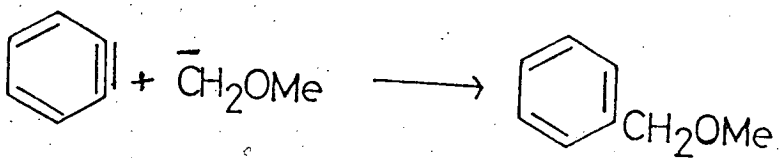
15 % 45 %

With simple olefins posessing an allylic hydrogen however, arynes give products attributable to the ene reaction[33,34]- again in analogy with the reaction of activated olefins.

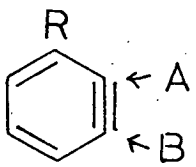


As had been shown from early methods of preparation, arynes react readily with nucleophiles of all kinds, thus with methanol[35], anisole is obtained, and with the acetonyl carbanion[36], benzyl methyl ether is the product.



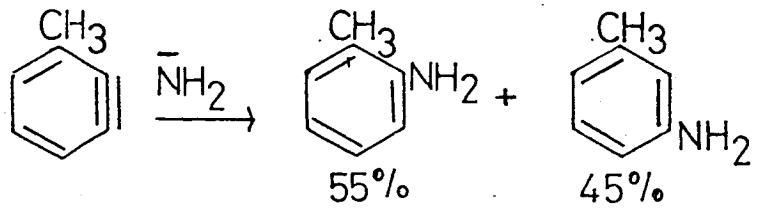


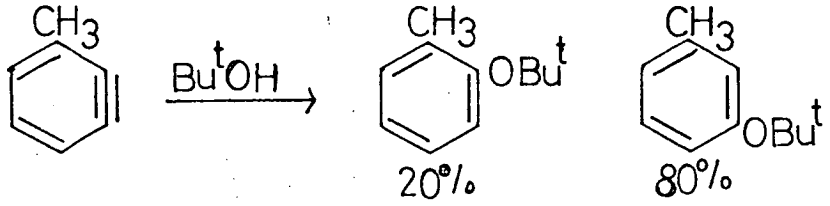
In the case of unsymmetrical arynes, there are two possible points of attack.



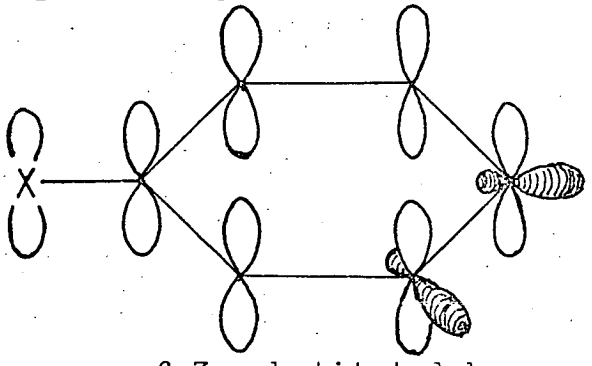
The ratio of products derived from attack at A or B will be dictated by steric and electronic effects - steric effects only being predominant in the case of o-arynes - and by the

size and nucleophilicity of the attacking reagent. Thus, the addition of the bulky t-butoxide anion to a 3-monosubstituted benzyne[37] was found to give a lower percentage of o-addition than would have been expected for the addition of an amide anion.





This was attributed to steric hinderance to addition. It must be remembered that the reactive centres in an aryne lie in sp^2 orbitals which are orthogonal to the π-system, 7, thereby experiencing only second order mesomeric effects.



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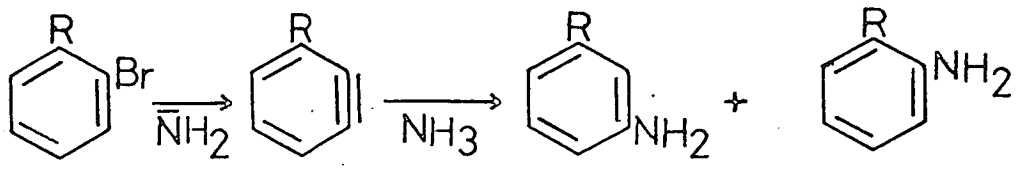
Thus, in the case of 3-substituted benzynes substitution will be controlled, in the absence of steric effects, by inductive effects which will swamp the weak mesomeric effects. These induction effects, transmitted through the σ-bonds will direct the attacking nucleophile to a position where the resulting charge on the nucleus will be best stabilised. Thus we can expect that a strong electron - withdrawing substituent will be m-directing and that a strongly electron- donating substituent will be o-directing.

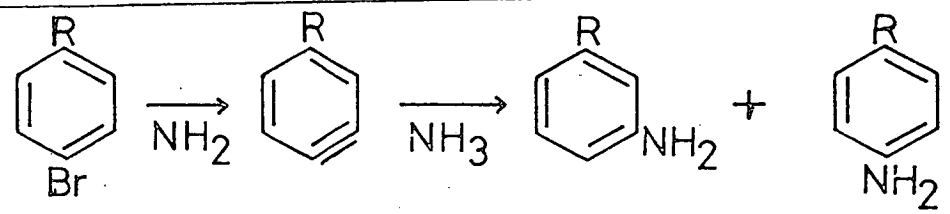
Table 1: Orientation of Amide Addition to 3- and 4- Substituted Benzenes.

Orientation to 3-substituted benzyne

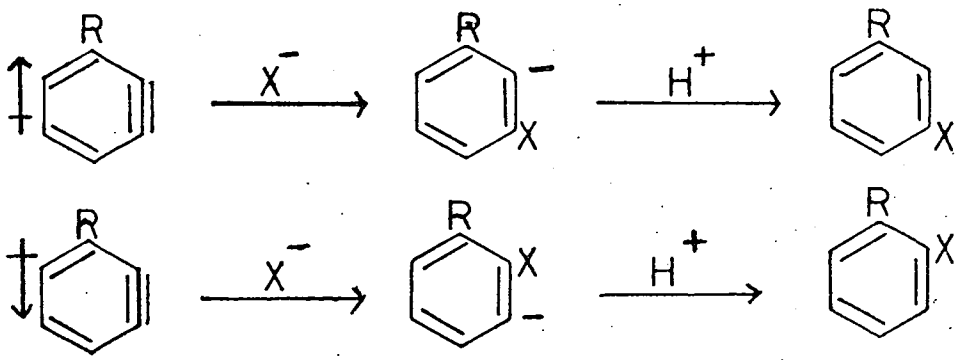


		Relative	Yields
R = CN	(--I,-M)	85-90	10-15%
OCH_3	(--I,++M)	95-100	0.5%
CH_3	(+I, +M)	45	55%
$\overline{O}$	(++I,++M)	10-15	85-90%

Orientation to 4-substituted benzyne

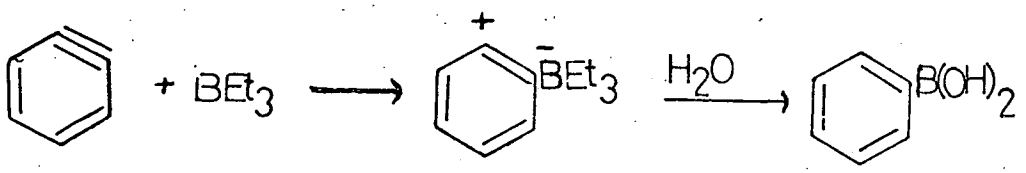


		Relative	Yields
R = CN	(--I,-M)	0-5	95-100%
OCH_3	(--I,++M)	45-50	50-55%
CH_3	(+I, +M)	60	40%
$\overline{O}$	(++I,++M)	100	0%



This effect is demonstrated in the work of De Graaf, den Hertog and Melger[38], who investigated the orientation of amide addition to monosubstituted benzynes. (Table 1). They also showed that in the case of 4-substituted benzynes the reactive centre was too far removed from the substituent for inductive effects to play such an important rôle, and in this case they found the second-order mesomeric effects becoming important, (table 1).

Electrophilic attack on benzyne is known to occur in few reactions. An example of this mode of attack is seen in the reaction of triethyl boron[39] and benzyne which, on subsequent hydrolysis, yields phenylboric acid.



2 FREE RADICALS

Background

The existence of free radicals was first postulated in the middle of the nineteenth century by Kolbe[40] and Frankland[41] who claimed to have observed free methyl and ethyl radicals. Molecular weight determination however proved these to be the dimers and it was not until 1900 that Gomberg[42], in his

attempts to prepare hexaphenyl ethane, described what he believed to be the triphenylmethyl radical. His postulate was later proved correct, but it was nearly thirty years before Paneth and Hofeditz[43] demonstrated the existence of methyl radicals in the gas phase by the pyrolysis of lead tetramethyl in an inert carrier gas. Moreover, they estimated the lifetime of these radicals to be of the order of one thousandth of a second.

Events began to move more quickly, and in 1934 Grieve and Hey[44] provided evidence for the formation of short-lived phenyl radicals in solution by comparison of the isomer ratios obtained from electrphilic aromatic substitution, and from the decomposition of N-nitrosoacetanilide. The free radical chain mechanism was proposed by Backstrom[45] in that same year to describe the autoxidation of benzaldehyde, and this same mechanism was applied by Hey and Waters[46], and Kharasch, Engelmann and Mayo[47] to the abnormal reaction of hydrogen bromide with olefins.

By this time free radicals had been accepted by most people to be genuine reaction intermediates. A new era in the understanding of reaction mechanisms had thus begun.

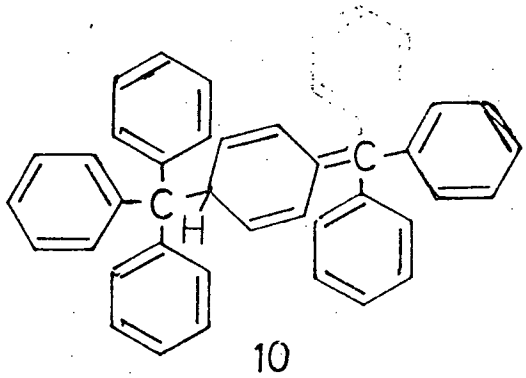
Structure And Reactivity of Radicals

Radicals can be described as being "electrically neutral atoms or groups of atoms having an unpaired electron". It is the ability of the unpaired electron to form a strong electron pair bond with a substrate which gives rise to the high reactivity of radicals. It must be stressed however, that their high reactivity does not indicate that they are unstable. Although radicals have short life-times, many have intrinsic thermodynamic stability. Thus

the methyl radicals of Paneth and Hofeditz[43] are stable despite their short half-life. Some radicals are unstable, however, as can be seen in the fragmentation of the acetoxy radical[48] to carbon dioxide and a methyl radical:

$$CH_3\,\underset{\underset{O}{\vdots}}{C} - \dot{O} \longrightarrow CH_3\cdot + CO_2$$

The triphenylmethyl radical, although stabilised by delocalisation, dimerises fairly rapidly with a half life of about one tenth of a second for a one per cent solution. Recent work[49] has shown that the dimer is in the methylene hexadiene structure, rather than the hexaphenylethane structure.



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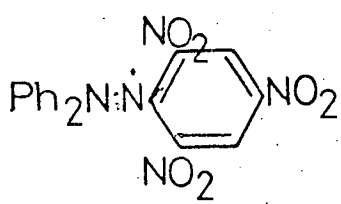
It is possible, however, to produce radicals which show little tendancy to dimerise as a result of their resonance stabilisation and steric hinderance. Examples of this group of free radicals are diphenylpicrylhydrazyl (8)[50], and galvinoxyl (9)[51] which may be kept exposed to the atmosphere for several weeks without appreciable deterioration.



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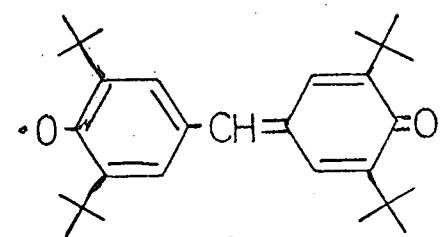
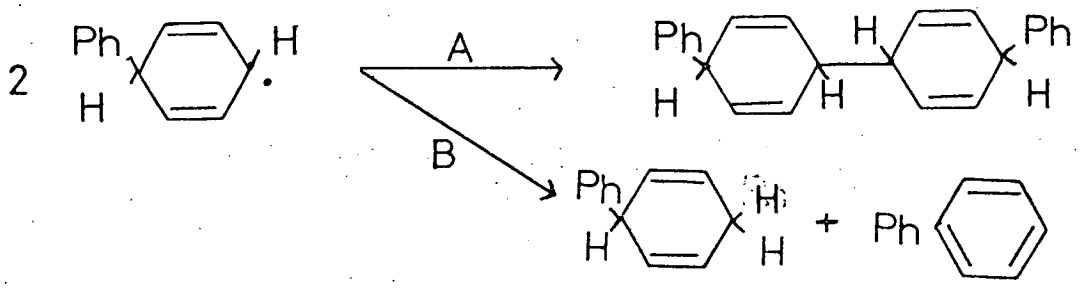


9

The chemical properties of radicals as might be expected, are in direct consequence of their posessing unpaired electrons.

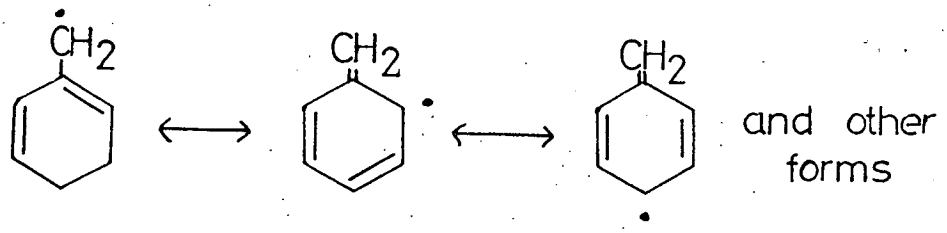
Thus the reactions of radicals will tend to proceed thereby reducing the inherent instability of the system.

The simplest reaction undergone by radicals is that of combination. This is the pairing of two radicals to form a neutral molecule and is most commonly noted when two radicals of the same species dimerise. This is exemplified by the dimerisation of the phenylcyclohexadienyl radical[52,53], A, which may also react with itself to form other stable products by disproportionation, B.



As the rate of these reactions is dependent upon the product of the radical concentrations, the reactions are characteristic of "long lived" radicals which are stabilised by delocalisation, or of "short-lived" radicals being produced in high local concentration.

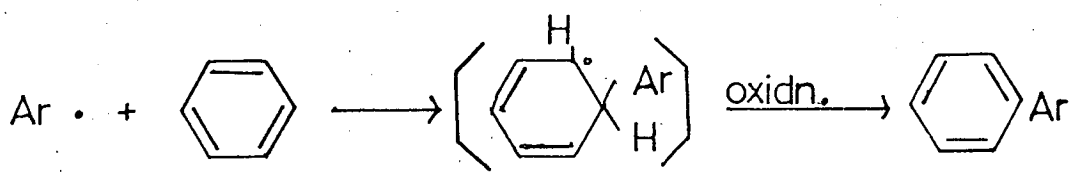
A typical example of a "long-lived" radical is the benzyl radical which is stabilised by delocalisation.



Thus in experiments attempting the homolytic aromatic substitution of cumene[54,55], a high proportion of 2,3-dimethyl-2,3-diphenylbutane- the dimerisation product of radicals produced by side-chain abstraction - was discovered. This effect was also noted for the rest of the series viz.

ethylbenzene and toluene[55,56]. Increased substitution by alkyl groups[57] was also found to enhance side chain abstraction. Similarly, Boeseken and Gelissen[58,59], on allowing dibenzoyl peroxide to decompose in chloroform, and carbon tetrachloride, noted the abstraction of hydrogen and chlorine by the phenyl radicals to form benzene and chlorobenzene.

By far the most common reaction of aryl radicals is that of aromatic substitution. Addition of a aryl radical to the substrate followed by oxidation of the arylcyclohexadienyl radical gives biaryl



Since the process of homolysis requires little charge separation in the transition state, it might be expected that it would be largely unaffected by polar effects. Similarly, one would expect homolytic aromatic substitution to be largely unaffected by the electronic effects which play such a great part in the orientation of electrophilic aromatic substitution. A penetrating study of the effect on orientation of substituents on the aromatic ring of the substrate and of the aryl radical was conducted by Hey and his coworkers[60], and others, who concluded that the insensitivity of radicals to polar effects could be used as a diagnostic test for radicals.

When generated in the presence of non-aromatic unsaturated compounds, radicals undergo addition. The anomalous addition of hydrogen bromide to allyl bromide studied by

Kharasch and May[47], and Hey[46] and his coworkers, was found to arise from peroxide initiation of a radical chain addition mechanism. The radical polymerisation of styrene again proceeds by addition of radicals in a chain process:

$$Ph\,CH{:}\,CH_2 + Ph\cdot \longrightarrow Ph\,\dot{C}H\,CH_2Ph \xrightarrow{RX} Ph\text{-}\overset{X}{C}HCH_2Ph + R\cdot$$

$$\downarrow Ph\cdot CH = CH_2$$

$$Ph - \dot{C}H - CH_2 - \overset{Ph}{C}H - CH_2Ph$$

Radicals, as has been said before, may be unstable on genesis, achieving a more stable state by <u>fragmentation</u> as in the case of the acetoxy radical[48]. More uncommon is the process of <u>rearrangement</u> to another, more stable, isomeric form, for example, 1,2 aryl migration[61]:

$$Ph - \overset{CH_3}{\underset{CH_3}{C}} - \dot{C}H_2 \longrightarrow \dot{C} - \overset{CH_3}{\underset{CH_3}{C}} - CH_2Ph$$

<u>Generation of Aryl Radicals In Solution</u>

Homolytic fission of weak bonds can be readily achieved by thermal or photolytic means. Thus, the photolysis of weak aryl-atom bonds has successfully produced aryl radicals from diphenylmercury[76], tetraphenyl-lead[76], triphenylbismuth[77], and iodobenzene. It has been shown that thermal homolysis of bonds with a bond strength of up to $10 KJmol^{-1}$ can be achieved by heating to temperatures of up to 150°. Dibenzoyl peroxide and phenylazotriphenylmethane[62] decompose quite readily at fairly low temperatures to give phenyl radicals.

$$(Ph\,CO_2)_2 \xrightarrow{heat} PhC\dot{O}_2 \longrightarrow Ph\cdot + CO_2$$

$$Ph_3C.N{:}N.Ph \xrightarrow{heat} Ph_3C\cdot + N_2 + Ph.$$

It should be added that the decomposition of dibenzoyl peroxide in aromatic solvents revealed the interesting fact that not all the benzoyloxy-radicals had decomposed to phenyl radicals, as some benzoic acid and isomeric aryl benzoates were found in the reaction mixture.[63] In polycyclic compounds which are highly reactive towards radical substitution, ester formation is the major reaction[64,65]. Other routes to benzoyloxy radicals, and hence to phenyl radicals are the thermolysis of lead tetrabenzoate[66], phenyliodosobenzoate[67], and silver halide dibenzoates[68]. Allied to the decompostion of phenylazotriphenylmethane is that of 1-phenyl-3,3-dimethyltriazen which, although stable in refluxing benzene, decomposes when hydrogen chloride is bubbled into the solution to give phenyl radicals[69].

$$PhN{:}N.NMe_2 + HCl \longrightarrow Ph. + N_2 + NMe_2HCl$$

The Gomberg[70] reaction represented the first simple route to biaryls but the reaction had

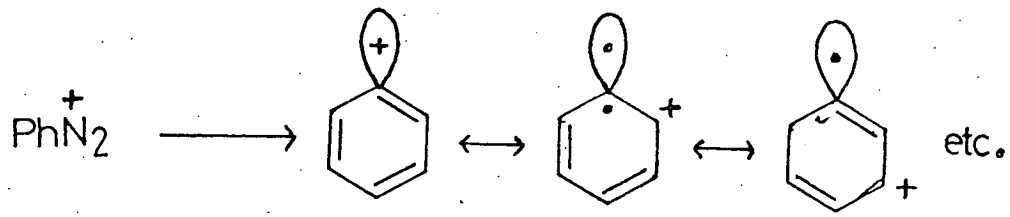
$$\overset{+}{PhN_2}\ \overset{-}{Cl} + NaOH_{(aq)} + PhH \longrightarrow PhPh + N_2 + Nacl + H_2O$$

the two great disadvantages of being heterogeneous and of producing much tarry material. Waters[71], and Waring and Abrams[72], found that suspensions of the diazonium chloride in aromatic solvents yielded phenyl radicals, probably by the homolysis of the covalent form of the salt.

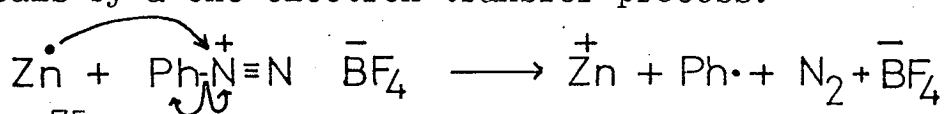
$$Ar\ \overset{+}{N_2}\ \overset{-}{Cl} \rightleftharpoons Ar\ N{=}NCl \longrightarrow Ar. + N_2 + .Cl$$

Abramovitch[73], in an analogous experiment with benzenediazonium fluoroborate, obtained mainly fluorobenzene and a small quantity of the isomeric biaryls. The isomer ratios, however, did not agree with those attributed to

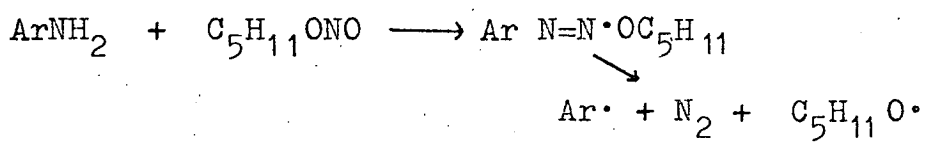
the intermediacy of an aryl radical and so a radical ion was postulated.



In studying the decomposition of benzenediazonium fluoroborate, Norman and Waters[74], discovered that a reducing agent such as zinc was required to aid the formation of phenyl radicals by a one electron transfer process:



Cadogan[75], devised a much simpler route to aryl radicals from aromatic amines by employing an in situ diazotisation technique with pentyl nitrite. The reaction is thought to proceed via homolysis of the diazoether.



In a similar vein, acylarylnitrosamines have proved to be a useful and important source of aryl radicals. These compounds will be discussed in detail in the following section.

3 ACYLARYLNITROSAMINES

Background

Fischer[78] first reported the synthesis of N-nitrosoacetanilide in 1876, achieved by passing nitrous fumes into a cold solution of acetanilide in acetic acid. Some years later, von Pechmann and Frobenius[79,80] acetylated benzenediazonium salts in alkaline solution to give the same product. This led to the suggestion of tautomerism[81]

between benzenediazoacetate and N-nitrosoacetanilide.

$$PhN(NO)Ac \rightleftharpoons PhN : N\cdot OAc$$

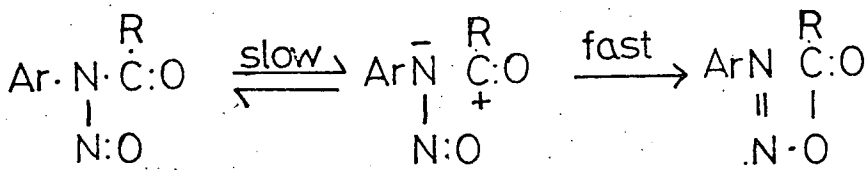
The study[82,83] of the decomposition of dry sodium arenediazotates in aromatic solvents in the presence of acetyl chloride, and acetic anhydride, to give the corresponding biaryls, led Bamberger[84,85] to decompose N-nitrosoacetanilide in benzene, producing biphenyl and acetic acid. The development of reactions of acylarylnitrosamines then lay in limbo until 1930 when Grieve and Hey[86] attempted to develop a synthetic route to biaryls using acylarylnitrosamines. Decomposition of dry solutions of N-nitrosoacetanilide in mono substituted benzenes yielded, like the Gomberg[70] reaction, biphenyls substituted at the 2- and 4- position irrespective of the substituent. This was incompatible with the known substitution pattern of electrophilic and nucleophilic aromatic substitutions, which prompted Grieve and Hey to postulate the production of phenyl radicals in the system. They argued that the phenyl radical is too short lived to dimerise, thus explaining the lack of biphenyl in reaction mixture resulting from the decomposition of N-nitrosoacetanilide in aromatic solvents other than benzene. Hey[86,87] and his coworkers conducted a kinetic investigation of the reaction, and established that in a wide range of solvents (except acetic acid), the first-order evolution of nitrogen was unchanged which led them to suggest that the rate-determining step for the decomposition was the homolysis of the benzenediazoacetate.

$$PhN(NO)Ac \rightleftharpoons PhN{:}NAc \xrightarrow{slow} Ph\cdot + N_2 + \cdot OAc$$

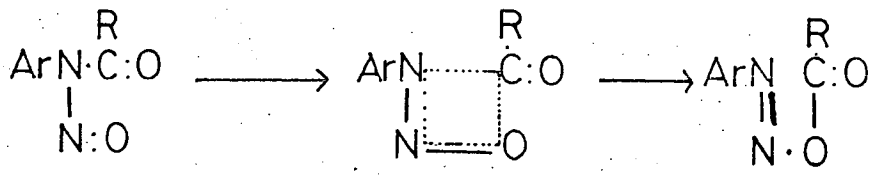
This suggestion was refuted by Huisgen and Horeld[88], who noted that N-nitrosoacetanilide coupled with 2-naphthol in a variety of solvents at the same rate as nitrogen had been evolved in the absence of 2-naphthol. Reasoning that the covalent diazotate was the common intermediate, they modified Hey's mechanism to make the rearrangement step rate-determining.

$$PhN(NO)Ac \xrightarrow{slow} PhN{:}N{\cdot}OAc \xrightarrow{fast} PhPh + N_2$$

The mechanism of this rearrangement became the centre of interest for both Hey[89] and Huisgen[90,91,92] with their respective coworkers. Two possible mechanisms were considered (schemes 4 and 5), and investigation of the effects of changing substituents in the acyl and aryl groups, among other things, led both teams of researchers to opt for the non-ionic intramolecular mechanism (scheme 5).

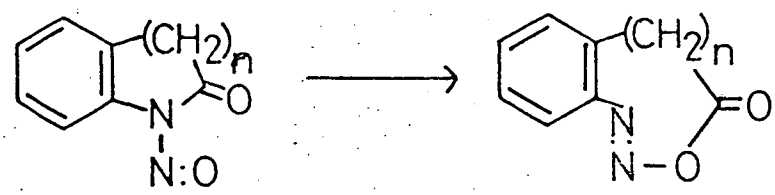


Scheme 4



Scheme 5

Since scheme 5 requires that the diazoester have the trans-configuration, Huisgen[92] conducted elegant experiments on the rearrangement of N-nitrosobenzolactams to cyclic-diazoesters (scheme 6), confirming that this was indeed the configuration of the diazoester. He found that, only when n was greater than or equal to three



Scheme 6

did the rearrangement occur. This was consistent with the fact that, for the diazoester in the trans-configuration, the smallest unstrained structure had a value of n equal to three.

The anomalous rate of decomposition in acetic acid, noted by Hey, was thought to occur for two reasons [88,89,93]. It was thought that denitrosation of the N-nitrosoacetanilide was occuring in a bimolecular reaction with acetic acid, and it was considered that the covalent diazotate might undergo hererolytic fission,

$$PhN(NO)Ac \rightleftharpoons Ph\overset{+}{N}_2\ \overset{-}{O}Ac$$

which would be favoured in acetic acid solution thus reducing the concentration of the covalent diazotate. The diazonium salt so produced would decompose slowly to yield phenyl acetate and nitrogen. De Tar[94] took this idea further by suggesting that the diazonium cation existed even in non-polar solvents and that azo coupling went via this diazonium cation rather than the covalent diazoester (scheme 7).

$$PhN(NO)AC \xrightarrow{\text{slow}} PhN{:}NOAc \xrightarrow{\text{fast}} Ph\cdot + N_2 + \cdot OAc$$

$$\Big\Downarrow \text{very fast}$$

$$Ph^{+} + N_2 \xleftarrow{\text{slow}} Ph\overset{+}{N}_2\ \overset{-}{O}Ac$$

scheme 7

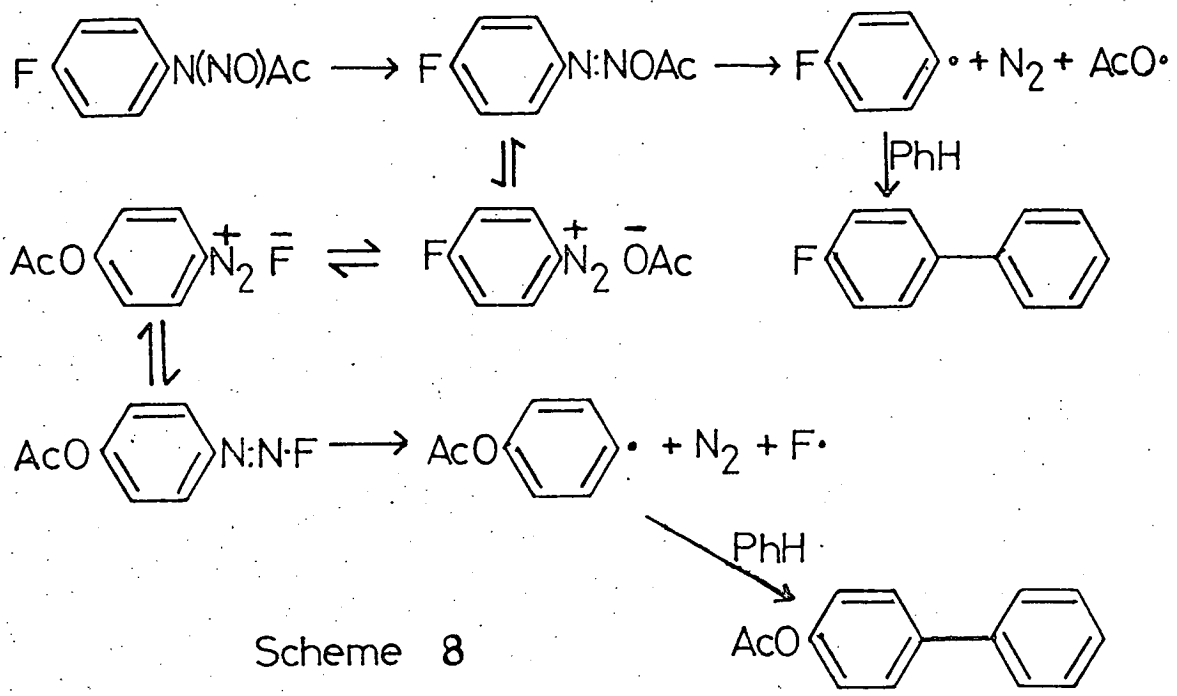
This suggestion arose from the fact that, N-nitrosoacetanilide, when decomposed in methanol under neutral conditions or in the presence of sodium acetate, gave benzene and formaldehyde[86]. Under acidic conditions, anisole was formed, which De Tar suggested found its

genesis in the formation of phenyl carbonium ions in solution. Thus he proposed a scheme in which the course of the decomposition would be governed by the solvent used. In methanol with sodium acetate, the diazoacetate was favoured, which decomposed to give phenyl radicals and hence benzene and formaldehyde. The acidic solution would favour the formation of the phenyl carbonium ion. The fact that appreciable quantities of carbon dioxide were only produced when acetic anhydride was used as solvent for the decomposition, led De Tar to suggest that, in all other solvents, the acetoxy-radical had a long enough lifetime to react before it fragmented.

De Tar's mechanism was challenged by Huisgen and Nakaten[90], who decomposed o-methyl-N-nitrosoacetanilide in chloroform to yield indazole in almost quantitative yield. Decomposition in ethanol both of N-nitrosoacetanilide and o-methyl-N-nitrosoacetanilide gave high yields of acetaldehyde, with little indazole being formed in the latter case. This indicated that the oxidation had been by some nitrogen-containing species which, in chloroform, had cyclised to indazole. This was in disagreement with De Tar's suggestion that the phenyl radical took the rôle of oxidising agent.

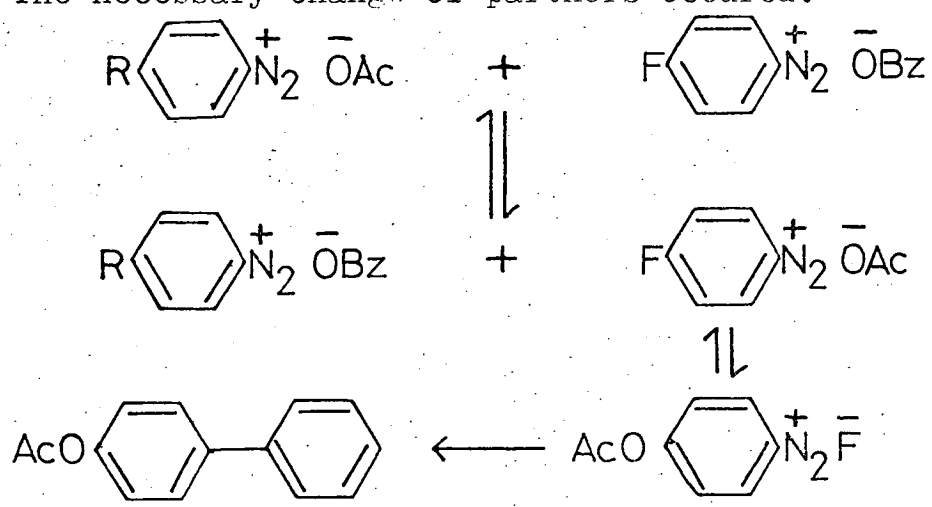
Suschitzky[95,96] and his coworkers demonstrated that the decomposition of o-and p-fluoro-N-nitrosoacetanilides and benzanilides in benzene yielded not only 2-and 4-fluorobiphenyls, but also comparable amounts of 2- and 4- acetoxybiphenyls. Neither fluorine in the m-position nor the other halogens in any position were displaced.

Suschitzky argued that this could be explained by the formation of ion pairs and the subsequent displacement of fluorine by the nucleophilic anion (scheme 8).



Scheme 8

The generality of this ion pair formation was demonstrated in crossover experiments (scheme 9) using p-fluoro-N-nitrobenzanilide and other substitued N-nitrosoacetanilides. The necessary change of partners occured.



Scheme 9

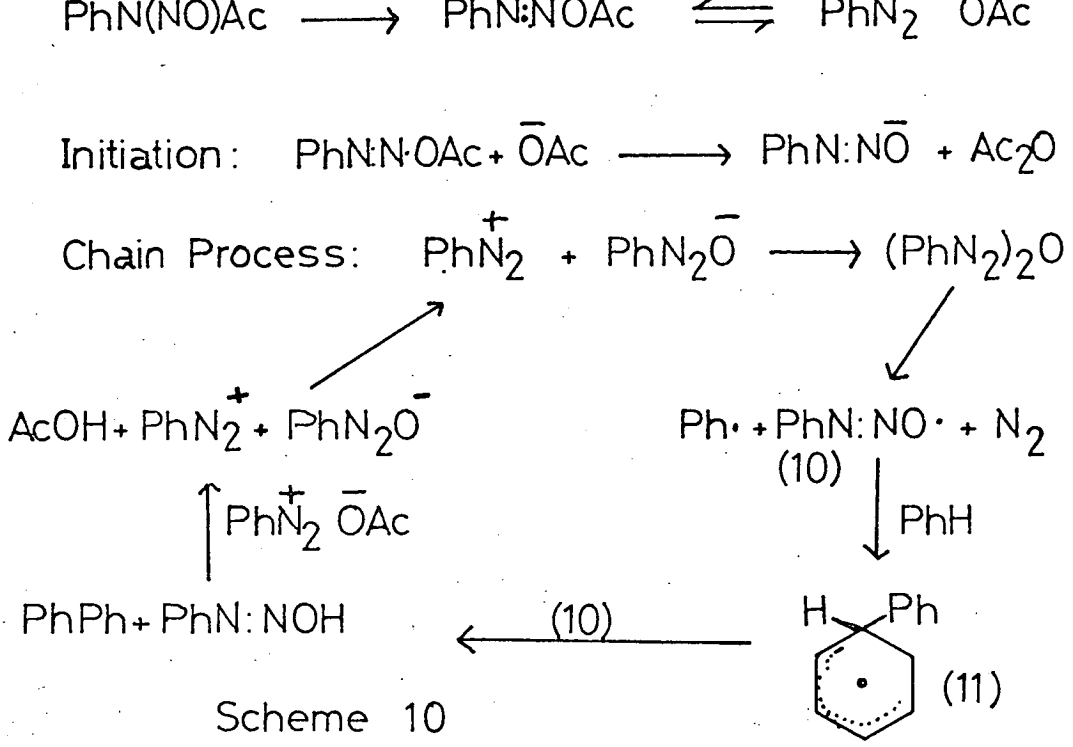
Still unexplained was the lack of dihydrobiaryls in the reaction mixtures of the decomposition of acylaryl-nitrosamines in aromatic solvent. The decomposition of

diaroyl peroxides in benzene had been shown[97] to produce products derived from disproportionation and dimerisation of the arylcyclohexadienyl radicals[52,53] - dihydrobiaryls and quateraryls. Eliel[97] and his collaborators could not find these compounds in the product mixture from the decomposition of N-nitrosoacetanilide in benzene, and suggested a "caged" reaction mechanism for the decomposition. He subsequently withdrew[98] this theory on discovering that N-nitrosoacetanilide, when decomposed in benzene containing iodine in low concentration, gave high yields of iodobenzene.

What was needed to explain this anomaly was an efficient oxidising agent to oxidise the arylcyclohexadienyl radical. The acetoxy radical, previously thought to be the executor of this step, had been found to be unstable[48] under the reaction conditions, decomposing to carbon dioxide and a methyl radical. The recent work in this field has centred around the search for this oxidising agent.

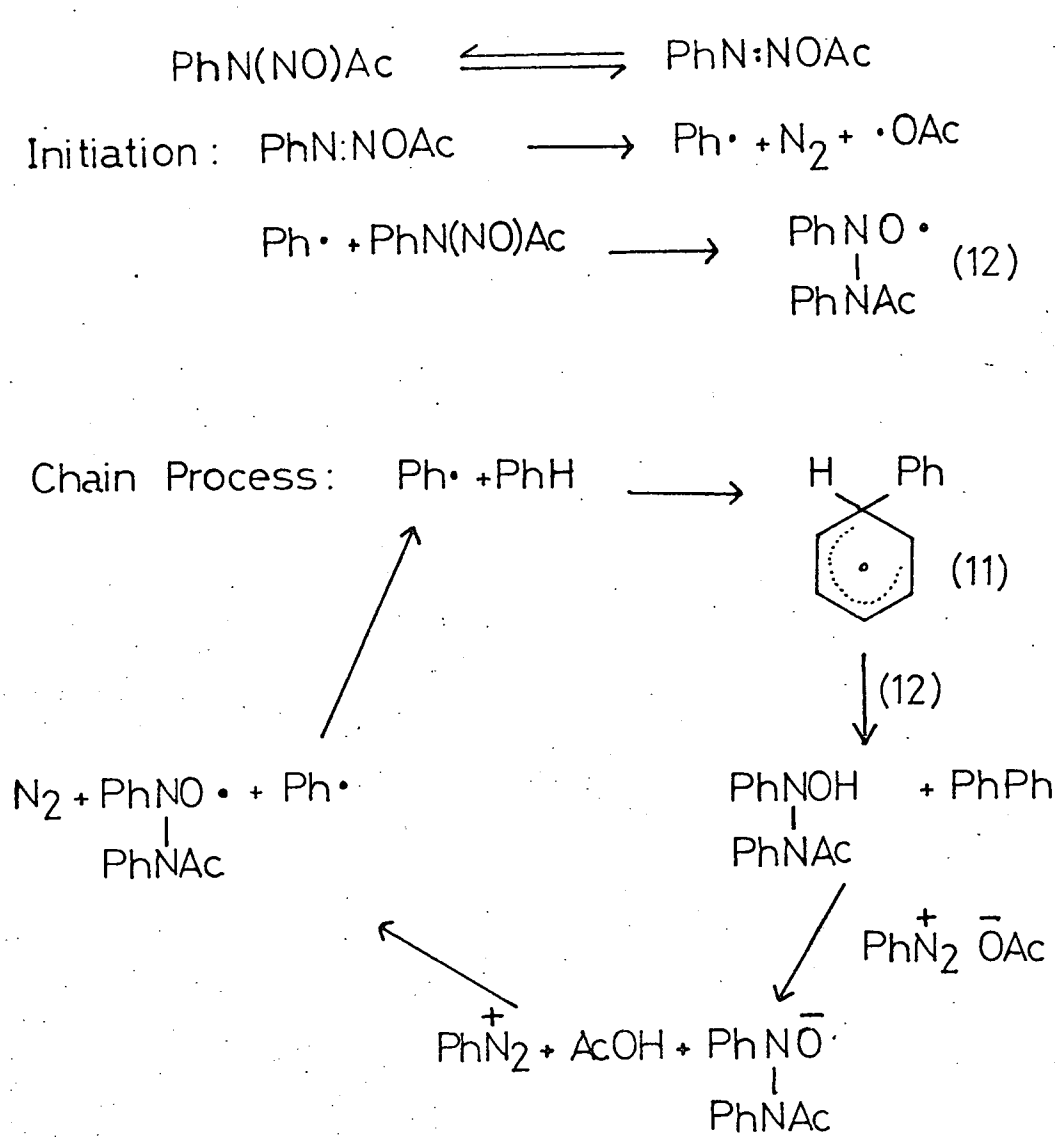
Recent Results

In 1964 Ruchardt and Freudenberg[99] proposed what appeared to be the perfect explanation of the reaction (scheme 10).



Scheme 10

This scheme contains the necessary oxidising agent, the π-type phenyl diazotate radical,10, capable of abstracting hydrogen and thus of oxidising the arylcyclohexadienyl radical, 11. The scheme neatly explains the formation of acetic acid, not from an acetoxy radical, but from the acetate ion via a chain process. Ruchardt[99,100] supported his mechanism with the report of a long-lived e.s.r. signal when the decomposition was allowed to take place in the cavity of an e.s.r. spectrometer. This signal he assigned to the phenyl diazotate radical. Hey and Perkins and their collaborators[101], however, suggested that the signal was in fact due to a nitroxide, (N-phenylacetamido) phenyl nitroxide, PAPN, (12), produced by the scavenging of a phenyl radical by N-nitrosoacetanilide (scheme 11). Synthesis of the PAPN radical from nitrosobenzene and N-bromoacetanilide by Chalfont and Perkins[102] followed by two further independant syntheses[103], produced a compound giving an e.s.r. signal identical to 12.

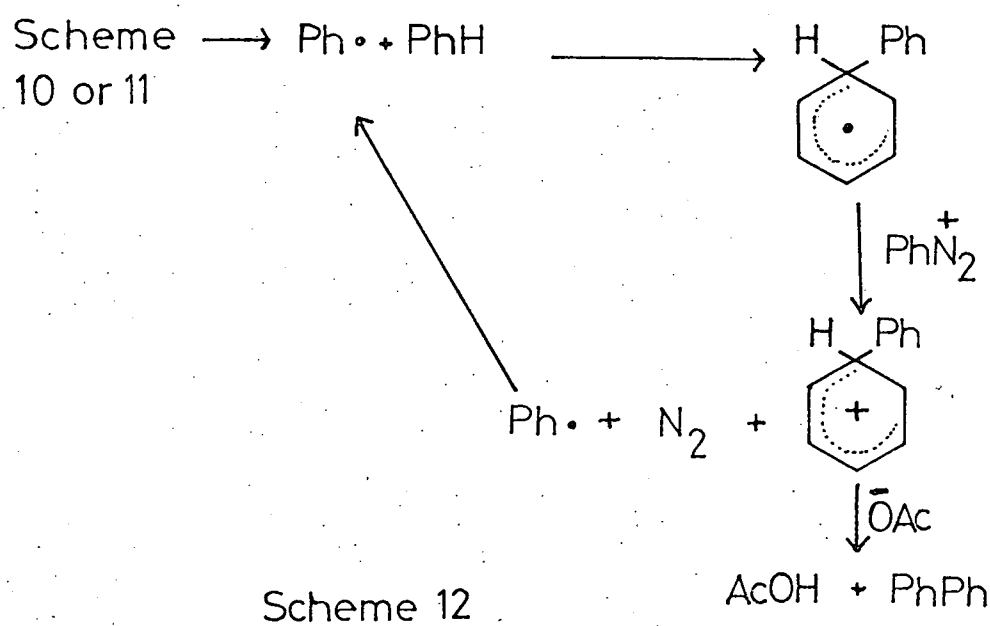


Scheme 11

On this evidence, Chalfont and Perkins proposed a new mechanism based on that of Ruchardt, but employing the PAPN radical as chain carrier (scheme 11) thereby combining the advantages of the Ruchardt mechanism with those offered by an authenticated free radical.

In 1969 Cadogan, Paton and Thompson[104] noted that the signal attributed to the PAPN radical was not present in all solvents as should have been the case if scheme 11 were to represent the major route of the reaction. Furthermore, they found in all solvents a

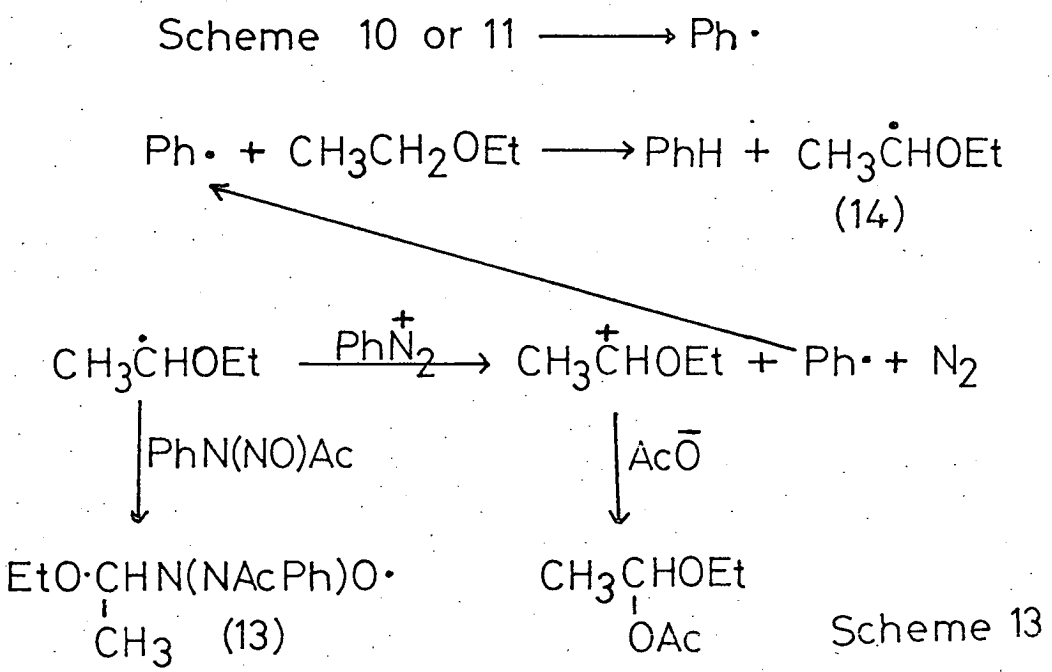
weak signal which, it appeared, had been overlooked by previous workers. This signal they attributed to a σ-phenyldiazotate radical, from analogy with the closely-related iminoxy radicals[105], thus favouring Ruchardt and Freudenberg's scheme 10 over that of Chalfont and Perkins, scheme 11, but allowed that, in cases where both e.s.r. signals appeared, both schemes might have been operative. Cadogan, Paton and Thompson[106] also proposed that once initiation by scheme 10 or 11 had occured, a simple chain process involving a redox reaction between the arylcyclohexadienyl radical (11) and unchanged diazonium cation could represent the major pathway of the reaction (scheme 12). This scheme was proposed in analogy with the postulated reaction of N-nitrosoacetanilide and diethyl ether[107].



Scheme 12

It had been noted in 1964 by Denny and his coworkers[108] that this reaction gave benzene (52%), 1-ethoxyethyl acetate (22%) and acetaldehyde (50%). This could not be explained until an e.s.r.[107] study had been conducted,

which showed only a weak signal due to PAPN and a signal attributed to the radical 13 (scheme 13). The signal from the diazotate was absent. The precursor to radical 13 was taken to be the radical 14 which, it was postulated, underwent a redox reaction with the diazonium cation to give a phenyl radical, the chain carrier, and the

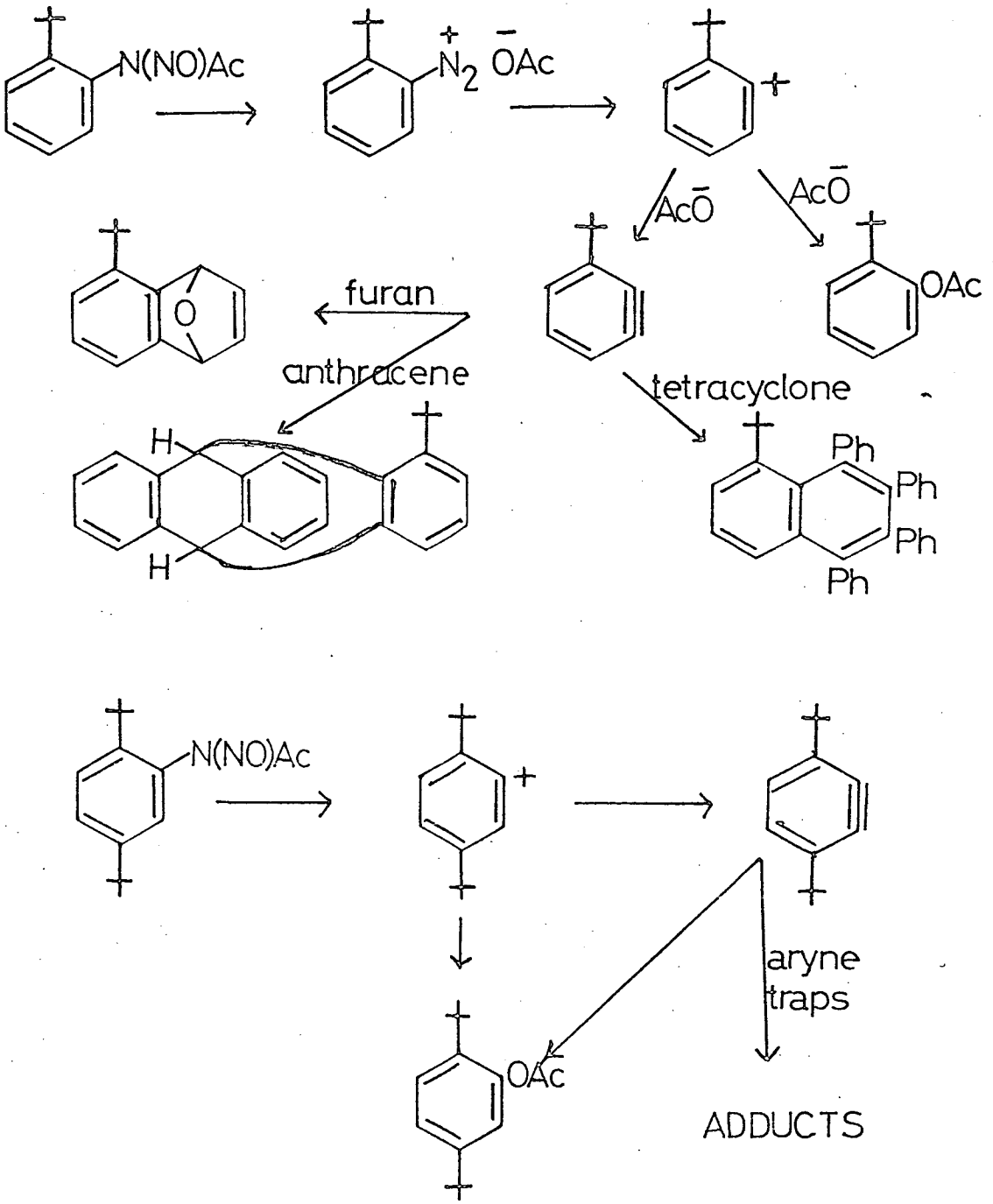


Scheme 13

∝-ethoxyethyl carbonium ion which was trapped by acetate ion to give the observed product. A similar electron transfer reaction had been postulated by Ruchardt and Werner[109] in the reaction of diazonium salts in 1,3-dioxolan.

The Question of Aryne Participation

The best representation of the mechanism of the decomposition of acylarylnitrosamines in aromatic solvents to give biaryls and acetic acid is probably that of scheme 12. It is far from being the overall mechanism of the decomposition however, as it has recently been shown that the acylarylnitrosamines give aryne adducts[110,111,114]

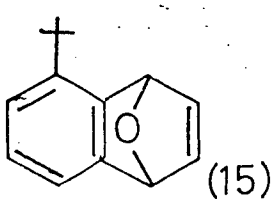

N(NO)Ac
N2 OAc
AcO
AcO
OAc
furan
anthracene
tetracyclone
H
H
Ph
Ph
Ph
Ph
N(NO)Ac
aryne
traps
OAc
ADDUCTS

Scheme 14

when decomposed in solutions containing aryne traps. The first hint of the existence of this new, and exciting facet of the decomposition of acylarylnitrosamines was not interpreted at first. Hey and his coworkers[110] observed that the decomposition of o-t-butyl-N-nitrosoacetanilide in benzene gave, unlike the p-isomer which behaved normally, isomeric t-butylbiphenyl acetates instead of the expected 2-t-butylbiphenyl. Cadogan and Hibbert[111] some time later showed that only the o- and m-t-butylbiphenyl acetates were present which they took to indicate the intermediacy of o-t-butylbenzyne. This was confirmed in trapping experiments with anthracene, and subsequently[112] with furan, and 2,3,4,5-tetraphenylcyclopentadienone. Competition reactions of o-t-butylbenzyne from an authentic source[106] and from o-t-butyl-N-nitrosoacetanilide gave similar rate ratios[113]. It was found that all the arynophiles suppressed the formation of the m-acetate, leaving the quantity of o-acetate virtually unchanged, which suggested rapid formation of the o-t-butylphenylcarbonium ion (aided by steric effects) followed by loss of a proton giving the aryne, or combination with an acetate ion (scheme 14). The fact that the yield of m-acetate only was affected by arynophiles led them to suppose that it arose from the addition of acetic acid to o-t-butylbenzyne - a reaction dominant in this case due to the steric suppression of the other normal side reactions of arynes by the bulky t-butyl group. This theory was endorsed by the fact that the

decomposition of 2,5-di-t-butyl-N-nitrosoacetanilide,[112] which has extreme steric shielding of the dehydro bond, gave 79% of the acetate, and reasonable yields of adducts when decomposed in benzene with and without arynophiles. This reaction turned out to be,not a special case as was first supposed, but the entrance to a new reaction study of the decomposition of acylarylnitrosamines when in 1967 it was shown that N-nitrosoacetanilide[114] itself, and other acylarylnitrosamines give aryne adducts with tetracyclone, anthracene, and 1,3-diphenylisobenzofuran.

The decomposition of o-t-butyl-N-nitrosoacetanilide[112] in benzene containing furan as aryne trap gave the adduct 1,4-dihydro-5-t-butyl-naphthalene-1,4-endoxide, 15. The decomposition of N-nitrosoacetanilide in benzene and furan gave,not the expected product of 1,4-dihydronaphthalene-1,4-endoxide, but 2-phenylfuran[114], 16.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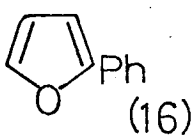
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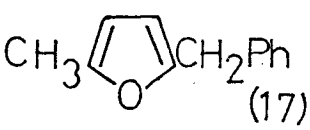
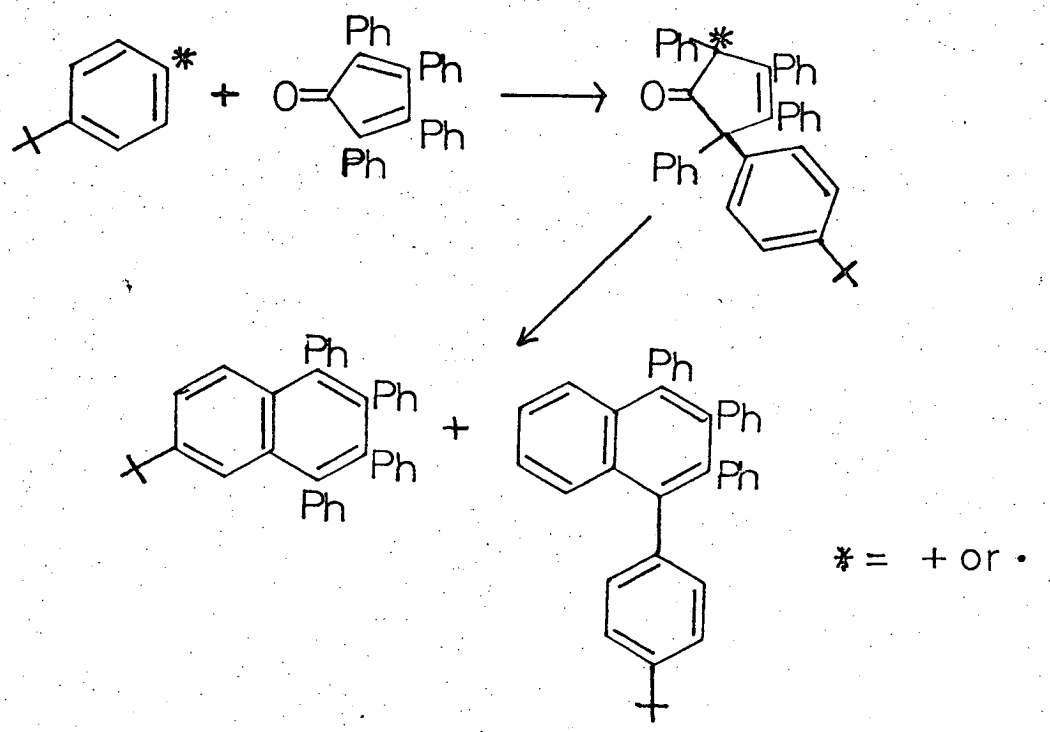

(17)

Also when decomposed in 2,5-dimethylfuran[115], 2-benzyl-5-methylfuran was the product,17.It was also found that the presence of furan suppressed the formation of adducts with other arynophiles that were present - a property not shown by tetrahydrofuran[114] and therefore not attributable to the ring oxygen. Furthermore, it had been shown that only in the case of o-t-butyl-N-nitrosoacetanilide had cine substitution products (the m-acetate) been detected.

Doubts began to arise as to whether a true aryne could be compatible with all these anomalies. Harger[116] had shown that, in the case of the reaction of p-t-butyl-N-nitrosoacetanilide with tetracyclone, the attack had been bidentate, since the lack of 1-(p-t-butylphenyl)-2,3,4-triphenylnaphthalene in the reaction products precluded monodentate attack by a carbonium ion or radical (scheme 15).

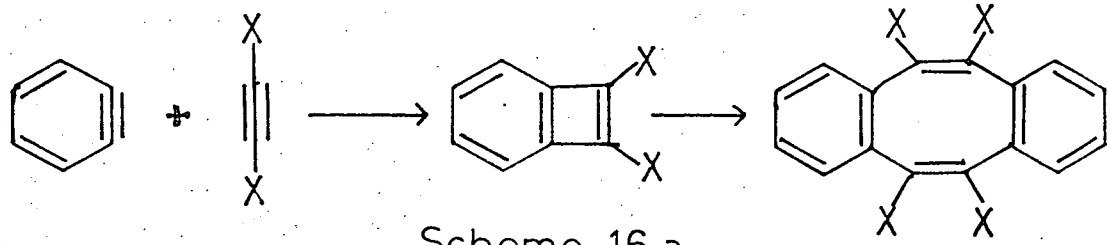


Scheme 15

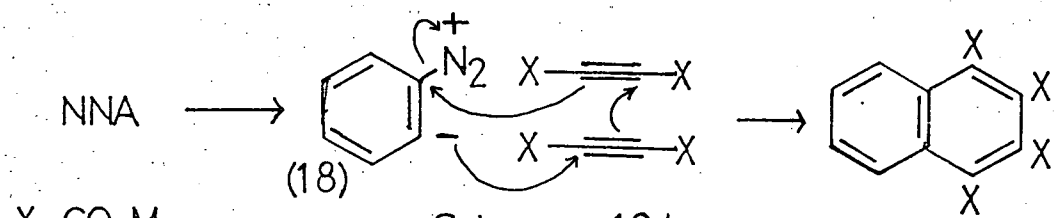
Cook[116] has shown that, for a series of arynophile pairs (except furan), the competition ratios of true benzyne, and of benzyne generated from N-nitrosoacetanilide, are the

same. Both of these points favour the intermediacy of arynes in the decomposition of acylarylnitrosamines. Cook[117], however, also showed that benzyne generated from anthranilic acid and pentyl nitrite reacted with dimethyl acetylenedicarboxylate to give a low yield of the dibenzocyclo-octatetraene (scheme 16a) whereas N-nitrosoacetanilide gave tetramethylnaphthalene-1,2,3,4-tetracarboxylate (scheme 16b).

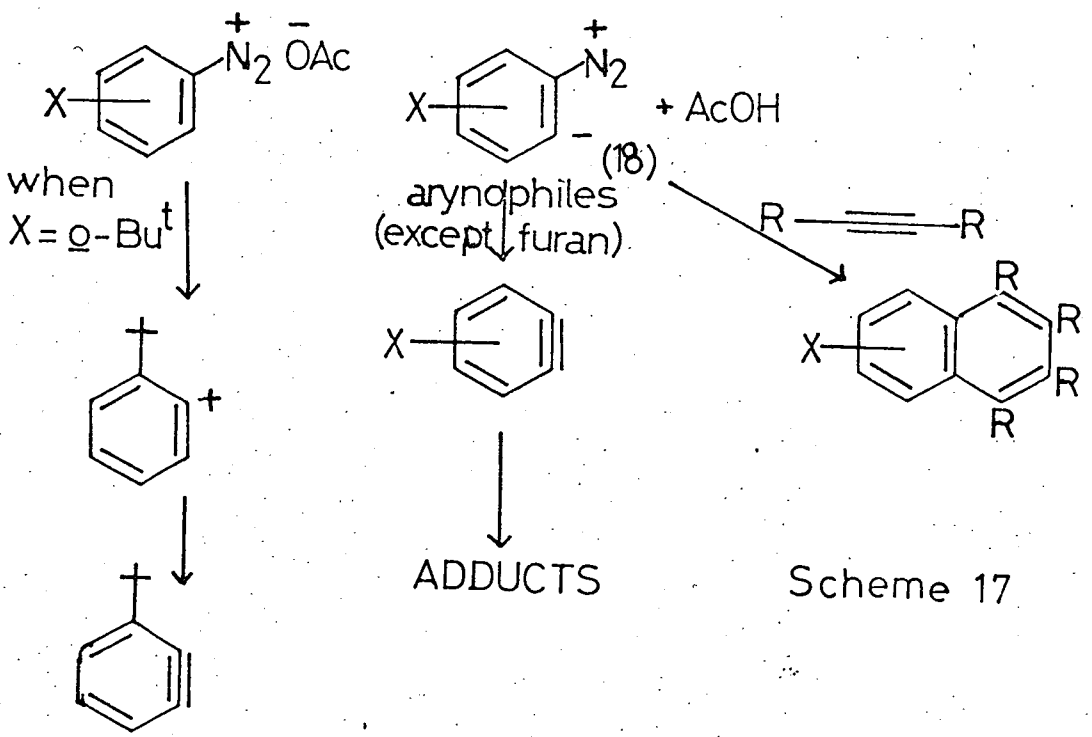
This has led to a revised decomposition mechanism (scheme 17) incorporating a new aryne precursor, 18, in equilibrium with the diatonium cation[117,118].



Scheme 16 a



Scheme 16 b



Scheme 17

This "arynoid" species can be trapped by dimethyl acetylenedicarboxylate thus explaining the anomolous product (scheme 16).

The anomalous behaviour of N- nitrosoacetanilide in furan was explained in terms of π -donation reducing the acidity of the o-protons and/or fast removal of the diazonium acetate ion pair by the pathway to normal radical products[118]. The o-t-butyl- case can be explained in terms of a steric acceleration of the loss of nitrogen from the diazonium cation thus causing this process to precede the loss of the o-proton.

PROGRAMME OF RESEARCH

The discovery that N-nitrosoacetanilide gave abnormal products in furan and 2,5-dimethylfuran, was in direct conflict with the fact that competition ratios obtained from authentic benzyne and from N-nitrosoacetanilide were comparable. A study was required to find the reason for the anomalous products from furan, and more especially, 2,5-dimethylfuran.

Knowledge of the fact that water inhibits aryne formation from acylarylnitrosamines suggested that a new route to arynes from arylamines and pentyl nitrite might be feasable.

Both of these problems were investigated.

EXPERIMENTAL

Symbols and Abbreviations

M^+	mass of molecular ion
g.l.c.	gas liquid chromatography
m/100m	moles per 100 moles of starting material
m.p.	melting point
b.p.	boiling point
i.r.	infra-red
u.v.	ultra-violet
n.m.r.	nuclear magnetic resonance
s	singlet
d	doublet
t	triplet
g	quartet
c.i.d.n.p.	chemically induced dynamic nuclear polarisation
Rf	ratio of distance moved by the substance to the distance moved by the solvent front (in t.l.c.)

Gas Liquid Chromatography

Three instruments were used for analytical and quantitaive g.l.c. investigations; a Varian Aerograph 1520 B chromatograph, with flame ionisation detector, using 2m x 2.2mm i.d. packed columns; a Pye 104 chromatograph, with flame ionisation detector, using 1.5m x 4mm i.d. packed columns and a Griffin and George D.6. chromatograph with gas density balance, using 2m x 5 mm i.d. packed columns. Quantitative measurements were made using the D.6 instrument following the technique of Cadogan and Sadler[119], or using the 1520 B or 104 chromatographs after calibration of the instrument with known mixtures of authentic samples and internal standards, the technique being that described by Hibbert[120]. All authentic samples and internal standards were purified before use. For preparative g.l.c. a Pye 105 model 15, and the Griffin and George D.6. were used. In all cases the carrier gas was nitrogen, the flow-rates and split ratios being as recommended by the manufacturers. The following stationary phases, supported on 100-120 mesh celite were employed; neopentylglycol succinate (NPGS), polyethyleneglycol adipate (PEGA), fluorosilicone oil (QF-1), silicone grease (SE-30 and OV-1), silicone oil (SIL), Apiezon L grease (APL), and polyethyleneglycol (CAR).

Column Chromatography

The alumina used for column chromatography was Spence and Sons, grade H, 100-120 mesh (Brockmann activity =1).

The silica gel was M. and B. 60-120 mesh.

Dry Column Chromatography

Dry column chromatography was carried out after the method of Loev and Goodman[121] using Woelm dry column alumina (Brokmann activity = 3) treated with Woelm fluorescent indicator for short-wave u.v. (254 nm). Latterly we prepared our own alumina for dry column work from Spence and Sons, grade H, suitably deactivated by the method described by Loev and Goodman[121]. The columns were made up in "C" gauge, 2 inch nylon tubing from Walter Coles and Co.,Ltd., London, S.E. Glass tubes, i.d. 1.5 inches,were also used from time to time. After development, the columns were sliced (nylon), or extruded (glass), and the products were washed off with much ether.

Thin Layer Chromatography

Thin layer chromatograms were obtained on 0.3 mm layers of alumina (Merck, aluminium oxide G) or silica gel (Macherey, Nagel and Co., silica gel G). Components in the developed chromatograms were detected by their fluorescence in u.v. light or by their reaction with iodine.

Mass Spectroscopy

Mass Spectfa were obtained using on A.E.I. MS-902 mass spectrometer. Crude mixtures were analysed using an A.E.I. MS-20 mass spectrometer coupled to a Pye 104 gas chromatograph using helium as the carrier gas. Exact mass measurements were conducted on the MS-902 instrument. The use of mass spectrum/g.l.c. analysis to confirm the presence of compounds in reaction mixtures

was utilised in certain cases. The mass spectrum of the sample from the reaction mixture was compared with that of an authentic sample. The prominent peaks in the mass spectrum, together with their relative intensities, are given for each of the compounds confirmed by this technique in Appendices 1 and 2 (p.88)

Nuclear Magnetic Resonance Spectroscopy

A Perkin - Elmer model R-10 nuclear magnetic resonance spectrometer operating at a frequency of 60 MHZ, and a probe temperature of 35.5°, and a Varian HA-100 nuclear magnetic resonance spectrometer operating at a frequency of 100 MHz, and a probe temperature of 28° were used. Chemical shifts are recorded as τ values, in parts per million, tetramethylsilane being the internal reference. Spectra were obtained from 10-15% w/v solutions in carbon tetrachloride, or deuterochloroform. Searches for c.i.d.n.p. were conducted on the HA-100 instrument.

Infrared Spectroscopy

Perkin-Elmer models 257 and 337 were used for infrared spectroscopy, liquid samples being examined as thin films, and solid samples as melts or Nujol mulls.

Melting Points

Melting points of all new compounds were determined using a Kofler hot stage apparatus.

Elemental Analyses

Microanalysis were performed by Mr. J. Bews, University of St. Andrews and by Mr. B. Clark, Univ. of Edin.

Solvents and Reagents

Benzene, ether and petroleum ether (fraction with boiling point 40-60° unless otherwise stated), were purified by distillation and dried over sodium wire. Furan and 2,5-dimethylfuran were passed down a short alumina column, distilled, and stored over sodium wire. Cyclohexane was dried over sodium wire. Acetanilide was purified by recrystallisation from ethanol. Aniline was distilled from zinc dust at atmospheric pressure and stored at -15°. All other reagents were purified by distillation or recrystallation.

1 PREPARATION OF SUBSTITUED FURANS AND THIOPHENES

a 2,5-Dimethylfuran

2,5-Dimethylfuran was prepared by the method of Gaertner and Tonkyn[122] by the dehydration of acetonylacetone with acetic anhydride in the presence of anhydrous zinc chloride. The product was a colourless, mobile liquid b.p. 93-94° / 760mm (lit b.p. [122] 93-94° / 760mm).

b 2,3,4,5,-Tetramethylfuran

3,4-Dimethylhexane-2,5-dione was prepared by the method of Moore[123], by the decomposition of dibenzoyl peroxide in butan-2-one. This was ring-closed by the method of Gaertner and Tonkyn[122] to give the product N.m.r. ($CDCl_3$) : τ, 8.23 (s, 6H, 2- and 5- Me); 7.92 (s, 6H, 3- and 4- Me), b.p. 146-149° / 760 mm (lit 146-148° / 748 mm[122]).

c 2,5-Dimethyl-3-phenylfuran

After the method of Boberg and Schultze[124], nitroethane and benzaldehyde, were condensed to form β-nitro-β-methylstyrene, which was reacted with sodio

ethylacetoacetate and ring-closed to give 2,5-dimethyl-3-carbethoxy-4-phenylfuran. This was hydrolysed to the acid and decarboxylated in quinoline and copper chromite. Double distillation yielded 2,5-dimethyl-3-phenylfuran b.p. 115-116° / 9mm (lit bp [124] 117/11mm).

d 2,5-Di-t-butylfuran

Isobutylene was reacted with furan after the method of Brown and Wright[125] to give a mixture of 2-t-butylfuran and 2,5-di-t-butylfuran which was resolved by distillation. Isobutylene was prepared by the method of Davis[126]. B.p. of 2,5-di-t-butylfuran 60° / 11mm (lit[125] 61-62° / 16-17mm).

e 2-Methyl-5-phenylfuran

2-Methyl-5-phenylfuran was prepared by the method of March[127]. Phenacylacetylacetone was prepared from sodio acetylacetone and bromoacetophenone, being isolated via its copper complex, which was decomposed with sulphuric acid. The triketone was boiled with sodium hydroxide solution to form phenacylacetone which was ring-closed in glacial acetic acid with zinc chloride to yield crystals of 2-methyl-5-phenylfuran, m.p. 41° (lit[128] 41-42°).

f 2,5-Dimethyl-3,4-dicarbethoxyfuran

Diacetylsuccinic acid diethyl ester was prepared by the method described by Harrow[129], and was ring-closed by the method of Knorr[130], to give 2,5-dimethyl-3,4-dicarbethoxyfuran b.p. 155° / 11mm (lit b.p. 275.5° / 735mm) n.m.r. ($CDCl_3$) : τ, 8.7 (t, 3H, Me); 5.75 (q, 2H, CH_2); 7.62 (s, 3H, furan Me).

g 2-Benzoyloxymethylfuran

The ester was prepared following the method of Wissell and Tollens[131] as a yellow oil b.p. 108° / 0.1mm (lit b.p.[131] 272° / 760 mm) n.m.r. (CCl_4): τ, 4.8 (s, 2H, CH_2); 3.65 (complex, 2H, furan H_3 and H_4); 2.6 (4H) and 2.05 (2H) (complex, Ph and furan H_5).

h 2-(Benzoyloxymethyl) -5-methylfuran

5-Methylfurfural was prepared by the method of Scott and Johnson[132] and was reduced using sodium borohydride to the alcohol. 5-Methylfurfuryl alcohol (3g. 25 mmol) was dissolved in anhydrous ether (10ml) containing triethylamine (2.51g, 25 mmol). Benzoyl chloride (3.48g, 25mmol) was added slowly, and the reaction mixture was stirred overnight under an atmosphere of oxygen-free nitrogen. The reaction mixture was washed with water and then dried over magnesium sulphate. Evaporation of the mixture yielded a dark oil which on distillation gave 2-(benzoyloxymethyl)-5-methylfuran as a pale yellow oil (0.3g, b.p. 98-100° / 0.2mm) n.m.r. (CCl_4): τ, 7.7 (s, 3H, CH_3); 4.85 (s, 2H, CH_2); 3.72 and 4.12 (double d, 2H, furan); 2.6 (3H) and 2.0 (2H) (complex, Ph).

i 2,5-Dimethyl-3-phenylthiophene

3-Phenylhex-5-yne-2-one was prepared by the method of Reisch[133] and ring-closed by the method of Schultze[134] et al giving 2,5-dimethyl-3-phenylthiophene b.p.100° / 2mm (lit[134] 109 / 1.5mm) n.m.r. (CCl_4): τ, 7.6 (s, 6H, 2Me); 3.4 (broad s, 1H, H_4); 2.75 (broad s, 5H, Ph).

2 PREPARATION OF ARYNE TRAPS

a 2,3,4,5-Tetraphenylcyclopentadienone

Benzil (50g, 0.25 mol) and dibenzyl ketone (50g, 0.25 mol) were heated in ethanol (500 ml) to just below the boiling point. Potassium hydroxide (5g) in ethanol (50ml) was added slowly to the solution over 15 min and the reaction mixutre was boiled for 20 min under reflux conditions. The cooled solution was filtered and the precipitate recrystallised from benzene / ethanol (1:1) to give 2,3,4,5-tetraphenylcyclopentadienone (80g, 80%), m.p. 217° (lit[135] m.p. 218°)

b 9,10-Dimethoxyanthracene

This compound was prepared from anthraquinone by Meyer's[136] method in 55% yield, and was recrystallised from acetic acid m.p. 202° (lit[136] m.p. 202°)

c 1,4-Dimethoxyanthracene

1,4-Dimethoxy-9,10-dihydro-9,10-dihydroxyanthraquinone (10g) was warmed with titanous chloride (35g) in methanol (250ml) and poured into water (2000ml). Chromatography of the precipitate on alumina, eluting with benzene/petrol (1:4) gave, after recrystallisation from acetic acid, 1,4-dimethoxyanthracene[137] (7g, 80%) m.p. 136-137° (lit[137] 137°).

3 PREPARATION OF ORGANIC NITRITES

a Benzoyl and 4-Chlorobenzoyl Nitrites

Benzoyl nitrite was prepared from the reaction of nitrosyl chloride and silver benzoate in carbon tetrachloride[138] b.p. 40° / 0.6mm (lit b.p. 38° / 0.5mm).

The same method of Pritzkow and Nitzer[138] was used to prepare 4-chlorobenzoyl nitrite from nitrosyl chloride and silver 4-chlorobenzoate. M^+185 b.p. 62° / 0.7 mm.

b Pentyl Nitrite

Pentyl nitrite was prepared as described by Vogel[139] b.p. 103-104° / 760 mm (lit b.p.[139] 104/760 mm).

4 PREPARATION OF ACYLARYLNITROSAMINES

a General Preparation of N-nitrosoacetylarylamines

The acetylarylamine (74 mmol), potassium acetate (10g), and phosphorus pentoxide (1g) were stirred at 0° in a mixture of acetic acid (70ml) and acetic anhydride (30ml). Nitrosyl chloride (6g, 92 mmol) in a 30% w/v solution in acetic anhydride was added dropwise over 30 mins. The solution was stirred over a further 30 mins and poured into ice water (1.5l). The N-nitrosoacetylarylamine separated out either (i) as a solid or (ii) as an oil.

(i) Solid N-nitrosoacetylarylamines were filtered from the mixture, washed with much water, and pressed between filtre paper. The yellow powder was dried over phophorus pentoxide at 0.05 mm.

Prepared in this way were:

N-Nitrosoacetanilide m.p. 50° (lit[140] m.p. 50°)

4-Methoxy-N-nitrosoacetanilide m.p. 73-74° (lit[141] m.p. 83-84°)

4-Methyl-N-nitrosoacetanilide m.p. 70° (lit[89] m.p.77-78)

4-Carbethoxy-N-nitrosoacetanilide m.p. 48° (lit m.p.[142] 48-49)

All these compounds decomposed on melting.

(ii) Liquid N-nitrosoacetylarylamines were extracted into benzene (3 x 25 ml) which was then dried by shaking over magnesium sulphate for a few minutes and then over phosphorus pentoxide for a few minutes. 2,5-Dimethylfuran was added directly to these benzene solutions, and the decompositions described later were allowed to proceed.

Prepared in this way were;

3-Methoxy-N-nitrosoacetanilide

3-Methyl-N-nitrosoacetanilide

3-Carbethoxy-N-nitrosoacetanilide

b 4-Chloro-N-nitrosobenzanilide

A mixture of 4-chlorobenzanilide (10g, 48 mmol) acetic acid (100ml), acetic anhydride (100ml), and pyridine (30ml) was stirred at 0°. Nitrosyl Chloride (20g, 0.36 mol) in acetic acid (100ml) was added dropwise over 30 min, stirring was continued for a further 15 min, and the mixture poured into ice-water. After washing with much water, the yellow compound was dried between filtre papers and then over phosphorus pentoxide at 0.05 mm. The product (8g, 60%) had m.p. 74° (lit[143] m.p. 75°)

In all cases, the dryness of the acylarylnitrosamine was checked by i.r. spectroscopy.

5 MISCELLANEOUS PREPARATIONS

a Nitrosyl Chloride

This compound was prepared by the method of Morton and Wilcox[144] from the action of hydrochloric acid upon

sodium nitrite. The product was dissolved as a 30% w/v solution in acetic anhydride or carbon tetrachloride, and was stored at -15° in sealed flasks.

b Phenylazotriphenylmethane

This compound was prepared by the method of Gomberg,[145] and was obtained in 45% yield m.p. 110° (lit[145] $110-111^{\circ}$)

c 1-Ethoxy-1-phenylethane

Phenylmethylbromomethane and sodium ethoxide were reacted as described by Bergmann[146]. A low yield (10%) of 1-ethoxy-1-phenylethane b.p. $73-75^{\circ}$ / 25 mm (lit[146] b.p. 74-76 / 23 mm) was obtained.

d 4-Chlorobenzoic Anhydride

Thionyl Chloride and 4-Chlorobenzoic acid were reacted to give 4-chlorobenzoyl chloride which was converted to 4-chlorobenzoic anhydride by the method described by Vogel[139]. The product (90%) had m.p. $186-187^{\circ}$ (lit[139] m.p. $192-193^{\circ}$)

e Acylarylamines

(i) Acetylarylamines - These were prepared by the method described in Vogel[139] and the following were prepared:

4-methoxyacetanilide	m.p. 134°	(lit[147] m.p. $130-132^{\circ}$)
3-methoxyacetanilide	m.p. 80.5°	(lit[147] m.p. 81°)
4-methylacetanilide	m.p. 147°	(lit[147] m.p. 146°)
3-methylacetanilide	m.p. 66°	(lit[147] m.p. 65.5°)
4-carbethoxyacetanilide	m.p. 110°	(lit[147] m.p. 110°)
3-carbethoxyacetanilide	m.p. 84°	(lit[148] m.p. 84°)

(ii) Benzanilide and 4-chlorobenzanilide - These were prepared by the method of Vogel[139]

Benzanilide m.p. 164° (lit[147] m.p. 163°)

4-Chlorobenzanilide m.p. 201° (lit[147] m.p. 194°)

f Benzenediazonium Fluoroborate

This compound was prepared by the method described in Vogel[139] m.p. 118° (decomp) (lit[139] m.p. 119-120°)

6 REACTIONS OF N-NITROSOACETANILIDE WITH FURAN

a Reactions at Room Temperature

(i) N-Nitrosoacetanilide (2g, 12mmol) was dissolved in furan (25ml), which had been distilled from lithium aluminium hydride, and the mixture was allowed to react overnight. The reaction mixture was then heated slowly to the boiling point and was boiled under reflux for 1h. Examination by g.l.c. (2% CAR, 120°) using naphthalene as internal standard showed the presence of 2-phenylfuran (78.5 m/100m) and 1,4-dihydro-1,4-epoxynaphthalene (0.12 m/100m). Examination of the mixture by mass spectrum/g.l.c. (2% CAR, 120°) confirmed the presence of 2-phenylfuran by comparison of the spectrum obtained with that of an authentic sample (Appendix 1). The instrument was not sensitive enough to give a spectrum of the peak corresponding to 1,4-dihydro-1,4-epoxynaphthalene. Distillation of the bulk of the solution afforded a sample of 2-phenylfuran (1g) b.p. 99-101°/11mm (lit[149] b.p. 107-108°/18mm) whose i.r. (film) and n.m.r. (CCl_4) spectra were indistinguishable from those of an authentic sample.

(ii) The experiment described was repeated in the presence of the adduct 1,4-dihydro-1,4-epoxynaphthalene (0.045g, 2.5 m/100m of the N-nitrosoacetanilide added). Analysis by g.l.c. (2% CAR, 120°C) using naphthalene as internal standard showed the concentration of 1,4-dihydro-1,4-epoxynaphthalene to be unchanged.

(iii) To furan (12.5 ml) which had been distilled from lithium aluminium hydride, was added, every 30 min, one of ten batches of N-nitrosoacetanilide (0.1g, 0.6mmol) in furan (1ml). After the final batch had been added, the mixture was stirred overnight and then gently boiled under reflux for 1h. Analysis by g.l.c. (2% CAR, 120°) using naphthalene as internal standard showed 2-phenylfuran (78 m/100m) to be present. This was confirmed by mass spectrum/g.l.c. analysis (Appendix 1). No peak corresponding to 1,4-dihydro-1,4-epoxynaphthalene was found (0.1 m/100m would have been detected).

b Reaction at Elevated Temperature

A solution of N-nitrosoacetanilide (1g, 6mmol) in benzene (10ml) was added dropwise over a period of 45 min to a boiling mixture of benzene (10ml) and furan (10ml). The mixture was boiled under reflux for 1h, and examined by g.l.c. (2% CAR, 120°) using naphthalene as internal standard. 2-Phenylfuran (60.8 m/100m), biphenyl (9.5 m/100m) and 1,4-dihydro-1,4-epoxynaphthalene (5.5 m/100m) were detected. The presence of each of these compounds in the reaction mixture was confirmed by comparison of the mass spectra obtained by mass spectrum/g.l.c. analysis of the reaction mixture with those of authentic compounds (Appendix 1).

7 COMPETITION REACTIONS OF SOME SOURCES OF PHENYL RADICALS AND BENZYNE FOR BENZENE AND FURAN

The competition ratio $K^{furan}_{benzene}$ in each reaction was taken to be the ratio of the yields of 2-phenylfuran and biphenyl. In each experiment, the identity of the peaks corresponding to 2-phenylfuran and biphenyl was confirmed by mass spectrum/g.l.c. analysis.

a N-Nitrosoacetanilide

(i) N-Nitrosoacetanilide (0.67g, 4 mmol) was stirred overnight in an equimolar mixture (16.5ml, 0.2mol) of furan and benzene. The reaction mixture was then boiled under reflux for 1h, and examined by g.l.c. (2%APL, 120°). The competition ratio $K^{furan}_{benzene}$ was found to be 15.9

(ii) The above reaction was repeated in the presence of water (0.07g, 5 mmol). The competition ratio was unaffected.

b Benzenediazonium Fluoroborate

The boiling point of a mixture of acetic acid (0.05 ml), potassium acetate (0.5g), and an equimolar mixture (14.6g, 0.2 mol) of furan and benzene, was raised to 57° by application of an external pressure to the system of 145 mm above atmospheric pressure. The mixture was boiled under reflux and benzenediazonium fluoroborate (0.96g, 5 mmol) was added in three batches, with a 30 min time lapse between the addition of each batch. The temperature of the mixture was maintained at 57° for a further

2h, and the mixture was analysed by g.l.c. (2% APL,119°). The competition ratio $K^{furan}_{Benzene}$ was found to be 16.5.

c Phenylazotriphenylmethane

A solution of phenylazotriphenylmethane (4.35g, 12.5 mmol) in an equimolar mixture (18.25g, 0.25 mol) of furan and benzene was boiled under reflux for 48h, and analysed by g.l.c. (2% APL, 120°). The competition ratio $K^{furan}_{benzene}$ was found to be 1.9.

d Pentyl Nitrite and Aniline

(i) A solution of aniline (0.38g, 4 mmol) and pentyl nitrite (0.81g, 7 mmol) in an equimolar mixture (16.5 ml, 0.2 mol) of furan and benzene was boiled under reflux overnight. Examination by g.l.c. (2% APL, 120°) gave the competition ratio $K^{furan}_{benzene}$ to be 4.8.

(ii) A solution of aniline (0.38g, 4 mmol) and acetic anhydride (1.2g, 11 mmol) in an equimolar mixture (11.5 ml, 0.125 m) of furan and benzene was boiled under reflux. Pentyl nitrite (0.8g, 7 mmol) in an equimolar mixture (5 ml, 75 mmol) of furan and benzene was added dropwise over 1h. The mixture was boiled under reflux for 24h. Examination by g.l.c. (2% APL, 120°) gave the competition ratio $K^{furan}_{benzene}$ to be 5.4.

e 4-Chlorobenzoyl Nitrite and Acetanilide

A solution of acetanilide (0.515g, 4 mmol) in an equimolar mixture (10 ml, 0.12 m) of furan and benzene was boiled under reflux. A solution of 4-chlorobenzoyl nitrite (1.25g, 6.8 mmol) in an equimolar mixture (6.5 ml, 0.08 m) of furan and benzene was added dropwise over 1h,

and the mixture was boiled under reflux overnight. Examination by g.l.c. (2% APL, 120°) gave the competition ratio $K^{furan}_{benzene}$ to be 9.0.

8 REACTIONS OF SOME SOURCES OF ARYL RADICALS AND ARYNES WITH 2,5-DIMETHYLFURAN

Throughout this chapter, each reaction mixture recorded was examined by g.l.c. (2% CAR, 130°, 2% APL, 127°) to try and detect the presence of 2-benzyl-5-methylfuran, 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene, 2,5-dimethyl-3-phenylfuran and 5,5'-dimethylbifurfuryl (0.2 m/100m of each of these compounds would have been detected). The absence of any of these compounds from a reaction mixture will not be recorded for each reaction, only their presence. Those of the above compounds which are not mentioned in the report of a particular reaction may be considered to have found to be absent.

a Benzenediazonium Fluoroborate

Benzenediazonium fluoroborate (4.8g, 25 mmol) was added in three portions, with 30 min between each addition, to a vigerously stirred mixture of 2,5-dimethylfuran (2.4g, 25 mmol), anhydrous potassium acetate (2.5g, 25 mmol) and acetic acid (0.25 ml) in benzene (75 ml) at 60°. The mixture was stirred for a further 2h. Chromatography of the bulk of the reaction mixture on silica (90g) eluting with petroleum gave biphenyl (0.7g) m.p. and mixed m.p. 71°, the i.r. (film) spectrum was indistinguishable from from that of an authentic sample, and 2-benzyl-5-methylfuran (50 mg), n.m.r. (CCl_4) and i.r. (film) spectra were indistinguishable from those of an authentic

sample. Continued elution of the column with benzene/diethyl ether 1:1 gave a red oil (1.33g) which resisted all attempts at purification.

Quantitative examination of the reaction mixture by g.l.c. (2% CAR, 124°) with 2,5-dimethyl-3-phenylfuran as internal standard gave the yields, biphenyl (32 m/100m) and 2-benzyl-5-methylfuran (2 m/100m).

b Phenylazotriphenylmethane

A solution of phenylazotriphenylmethane (10.4g, 30.3 mmol) in 2,5-dimethylfuran (5.76g, 60 mmol) and benzene (28g, 0.36 mol) was boiled under anhydrous reflux conditions with an atmosphere of oxygen-free nitrogen. White crystals separated which on recrystallisation from benzene, were found to be tetraphenylmethane (90mg, 3.8 m/100m m.p. and mixed m.p. 294°). Found: C, 94.00; H, 6.25. Calc. for $C_{25}H_{20}$; C, 93.75; H, 6.25% i.r. (nujol) compared with that of an authentic sample. Distillation of the mixture left from the separation of the tetraphenylmethane gave a white solid b.p. 110-120°/12mm (0.5 g) which on recrystallisation from petroleum was proved to be biphenyl (mp and mixed mp 70.5°), i.r. (film) spectrum was indistinguishable from that of an authentic sample. A second fraction was collected from the distillation (b.p. 125-130° / 0.2 mm, 1 g) which was recrystallised from petroleum to give white crystals found to be triphenylmethane, m.p. and mixed m.p. 94°. Found C, 93.7; H, 6.3. Calc. for $C_{19}H_{16}$: C, 93.45; H, 6.55. I.r. (nujol) spectrum was indistinguishable from that of an authentic sample.

Examination of the reaction mixture by g.l.c. (2% NPGS, 117°; 3% QFI, 145-196°) using bibenzyl and phenyl benzoate as internal standards gave biphenyl (14 m/100m) and triphenylmethane (31 m/100m).

c Dibenzoyl Peroxide

A solution of dibenzoyl peroxide (7.26g, 30 mmol) in benzene (28g, 0.36 mol) and 2,5-dimethylfuran (5.7g, 60 mmol) was boiled under reflux for 3 days. White crystals of benzoic acid separated from the mixture on cooling, and these were collected from a portion of the reaction mixture and recrystallised from benzene m.p. and mixed m.p. 122°, i.r. (nujol) spectrum was indistinguishable from that of an authentic sample. The reaction mixture left from the removal of benzoic acid was washed with sodium bicarbonate solution, dried over magnesium sulphate and distilled. The distillate, a yellow oil (1.0g, b.p. 90°/0.2 mm), was identified as 2-benzoyloxymethyl-5-methylfuran. Found: C, 72.1; H, 5.8. $C_{13}H_{12}O_3$ requires C, 72.2; H, 5.6%. The n.m.r. ($CDCl_3$) and i.r. (film) spectra were indistiguishable from those of the sample prepared by another route (1 b).
A portion of the reaction mixture (37%) was washed three times with sodium bicarbonate solution, twice with water, and the aqueous layers were combined, acidified, and continuously extracted with ether to yield benzoic acid (1.67g, 126 m/100m). The organic layer was distilled to give 2-benzoyloxymethyl-5-methylfuran (1.58g, 68 m/100m).

An attempt was made to detect c.i.d.n.p. effects in this reaction. Dibenzoyl peroxide (0.1g) was placed in an n.m.r. tube with 2,5-dimethylfuran (0.5ml) and the spectrometer was adjusted to scan repeatedly the range 4.5-5.5 (the area in which the peak from the methylene group appears) at a temperature of 92°. No emission or enhanced absorption effects were observed in the appearance and growth of the methylene absorption signal.

d Pentyl Nitrite and Aniline

(i) Without acetic anhydride - A solution of pentyl nitrite (3.5g, 30 mmol), aniline (2.85g, 30 mmol), and 2,5-dimethylfuran (5.76g, 30 mmol) in benzene (28g, 0.36 mol) was boiled under reflux for 6h. Examination of the reaction mixture by g.l.c. (2% NPGS, 132°; 2% APL, 130°) with bibenzyl as internal standard, showed the presence of biphenyl (9 m/100m). This was confirmed by mass spectrum/g.l.c. examination.

(ii) With acetic anhydride - A solution of pentyl nitrite (0.9g, 7.7 mmol) in benzene (5ml) was added dropwise over 1h to a refluxing mixture of aniline (0.5g, 5.4 mmol), 2,5-dimethylfuran (0.96g, 10 mmol), and acetic anhydride (1.5g, 14.7 mmol) in benzene (10ml). The mixture was boiled under reflux overnight and examined by g.l.c. (2% APL, 107° and 145°; 2% NPGS, 130°). Biphenyl (10 m/100m) was shown to be present, and this was confirmed by mass spectrum/g.l.c. examination.

e 4-Chlorobenzoyl Nitrite and Acetanilide

4-Chlorobenzoyl nitrite (1.6g, 8.6 mmol) in benzene

(50ml) was added over 1h to a boiling mixture of acetanilide (0.675g, 5 mmol) and 2,5-dimethylfuran (0.96g, 10 mmol) in benzene (100ml). The reaction mixture was boiled under reflux overnight. Examination of the reaction mixture by g.l.c. (2% APL, 107°, 2% CAR, 110°) suggested the presence of biphenyl (64 m/100m), and 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene (2.0 m/100m). This was confirmed by mass spectrum/g.l.c. examination.(Appendix 1 and 2).

f Anthranilic Acid and Pentyl Nitrite

Anthranilic acid (1 g, 7.4 mmol) in benzene (30ml) was added dropwise to a boiling solution of 2,5-dimethylfuran (1.45g, 15 mmol) and pentyl nitrite (1.1g, 9.4 mmol) in benzene (4ml). The reaction mixture was boiled under reflux overnight and then examined by g.l.c. (2% NPGS 127°) with biphenyl as internal standard. 1,4-Dimethyl-1,4-dihydro-1,4-epoxynaphthalene (8m/100m) was shown to be present and this was confirmed by mass spectrum/g.l.c. examination (Appendix 2).

g N-Nitrosoacetanilide

(i) At room temperature with benzene as solvent - N-Nitrosoacetanilide (4.97g, 30.3 mmol) was allowed to decompose overnight in a solution of 2,5-dimethylfuran (5.8g, 60 mmol) in benzene (28g, 0.36 mol) at room temperature under anhydrous conditions and an atmosphere of oxygen-free nitrogen. The reaction mixture was boiled under reflux for 1h, and examined by g.l.c. (2% NPGS, 127.5°, 2% APL, 140°) with bibenzyl as internal standard.

2-Benzyl-5-methylfuran (27 m/100m) and biphenyl (6 m/100m) were shown to be present. Pure samples of biphenyl (m.p. and mixed m.p. 71°, i.r. (film) spectrum indistinguishable from that of an authentic sample), and 2-benzyl-5-methylfuran (n.m.r. (CCl_4) and i.r. (film) spectra were indistinguishable from that of an authentic sample, n.m.r. (CCl_4): τ , 2.87 (s, 5H, Ph), 4.29 (s, 2H, furan H_3 and H_4), 6.18 (s, 2H, methylene), 7.79 (s, 3H, Me)) were obtained by preparative g.l.c. (10% CAR, 186°). A portion of the reaction mixture (20%) was chromotographed on silica (40g) and eluted with benzene. A yellow oil (0.3g) which proved to be a mixture of biphenyl and 2-benzyl-5-methylfuran was obtained, followed by a red oil (0.1g) Found: C,70.6; H, 5.0; N, 18.1% All attempts to purify the oil further failed, but an exact mass measurement made of the parent ion (m+=304) gave a value of 304.132071 . $C_{18}H_{16}N_4O$ requires an exact mass of 304.132404. The i.r. (film) spectrum showed an absorption 1680 cm^{-1}.

(ii) In the presence of water at room temperature with benzene as solvent - N-Nitrosoacetanilide (1.25g, 7.5 mmol) was allowed to decompose at room temperature, overnight, in a solution of 2,5-dimethylfuran (1.45g, 15 mmol) in benzene (7g, 90 mmol) containing varying amounts of water. The reaction mixtures were then boiled for 1h and examined by g.l.c. (2% NPGS, 125°, 2% APL 145.5°) using bibenzyl as internal standard. The yields of biphenyl and 2-benzyl-5-methylfuran obtained are given below (Table 2).

Table 2: The effect of Water on the Decomposition of N-Nitrosoacetanilide in 2,5-Dimethylfuran/Benzene.

Quantity of water present (mmol)	: 0	3.8	7.5
Yield of biphenyl (m/100m)	: 7	2.9	1.3
Yield of 2-benzyl-5-methylfuran (m/100m)	: 27	0.5	0.3

(iii) At room temperature with t-butylbenzene as solvent - N-Nitrosoacetanilide (3.66g, 22.3 mmol) was allowed to decompose overnight at room temperature in a solution of 2,5-dimethylfuran (4.21g, 44 mmol) in t-butylbenzene (35.3g, 0.26 mol). The reaction mixture was then boiled under reflux for 1h. Distillation of a portion (33%) gave a pale yellow oil (0.3g, b.p. 30-60°/0.5 mm) leaving a tar (0.5g) in the flask. Chromatography of the oil on silica gel (30g), eluting initially with petroleum, and then with a mixture of petroleum/benzene 15:1, gave white crystals (70 mg) identified by their g.l.c. retention times (2% PEGA, 147°; 2% APL, 180°) as being a mixture of o-, m- and p-t-butylbiphenyls when compared with a standard mixture of the three isomers. The n.m.r. ($CDCl_3$) spectrum also proved to be comparable with that of an authentic mixture of the isomers. Continued elution of the column gave a pale yellow oil (0.17g) whose n.m.r. (CCl_4) and i.r. (film) spectra were indistinguishable from those of an authentic sample of 2-benzyl-5-methylfuran. Quantitative examination of the reaction mixture by g.l.c. (10% Sil, 180°) using naphthalene as internal standard gave 2-benzyl-5-methylfuran (17.3 m/100m), and g.l.c.

(2% APL, 183°) examination using terphenyl as internal standard gave o-t-butylbiphenyl (1.3 m/100m), m-t-butylbiphenyl (3.3 m/100m), and p-t-butylbiphenyl (1.5 m/100m).

(iv) In boiling benzene as solvent - A solution of N-nitrosoacetanilide (1.48g, 15 mmol) in benzene (4ml) was added dropwise to a solution of 2,5-dimethylfuran (2.88g, 30 mmol) in boiling benzene (10ml). The reaction mixture was boiled under reflux for a further 2h. Examination of the reaction mixture by g.l.c. (2% APL, 130°; 2% CAR, 130°) with bibenzyl as internal standard showed the presence of 2-benzyl-5-methylfuran (2.4 m/100m), biphenyl (5 m/100m) and 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene (0.04 m/100m). The presence of each of these was confirmed by mass spectrum/g.l.c. examination. Also present in the g.l.c. chromatogram was an unknown peak with retention times 0.91 (2% APL 140°) and 1.2 (2% CAR, 130°) relative to 2-benzyl-5-methylfuran. Mass spectrum/g.l.c. examination of this compound gave M^+ 190 with a large half mass at 95 (Appendix 2). Distillation of a portion (68%) of the reaction mixture gave a yellow oil (0.25g; b.p. 100-120/18mm), which on g.l.c. (2% APL, 140°) examination proved to be a mixture of biphenyl, 2-benzyl-5-methylfuran and the unknown substance which, from the mass spectral evidence, was thought to be 5,5'-dimethylbifurfuryl. A mass spectral examination of the mixture revealed the highest mass present to be 190. An exact mass measurement of this peak gave

a value of 190.099254. $C_{12}H_{14}O_2$ requires 190.099373. The n.m.r. ($CDCl_3$) spectrum of the mixture gave, in addition to the aromatic absorption, absorptions at τ, 4.2 (s, 6H, 3xfuran H_3 and H_4); 6.15 (s, 2H, CH_2 from 2-benzyl-5-methylfuran); 7.15 (s, 3.6H, CH_2 from 5,5^1-dimethylbifurfuryl); 7.8 (s, 9H, $3CH_3$). G.l.c. examination (2% APL, 130°) with bibenzyl as internal standard gave the yield of 5,5^1-dimethylbifurfuryl to be 3.2 m/100m.

i N-Nitroso-4-chlorobenzanilide

N-Nitroso-4-chlorobenzanilide (2g, 7.7 mmol) was allowed to decompose at room temperature for 12h in a solution of 2,5-dimethylfuran (1.44g, 15.5 mmol) in benzene (7g, 90 mmol). The reaction mixture was then heated slowly to the boiling point and boiled under reflux for 1h. Examination of the reaction mixture by g.l.c. (2% NPGS, 125°; 2% APL, 140°) showed the presence of 2-benzyl-5-methylfuran (30 m/100m) and 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene (1 m/100m). The presence of these compounds was confirmed by mass spectrum/g.l.c. analysis (Appendix 2).

h Other N-Nitrosoacetylarylamines

General Method - The N-nitrosoacetylarylamine (30 mmol) was allowed to decompose overnight in a solution of 2,5-dimethylfuran (5.8g, 60 mmol) in benzene (28g, 0.36 mol) under anhydrous conditions and an atmosphere of oxygen-free nitrogen. The reaction mixture was then boiled under reflux for 1h. In the case of liquid N-nitrosoacetylarylamines, the benzene solution of the

compound obtained from the preparation (4 a (ii) was added to 2,5-dimethylfuran, the quantity of the nitrosamide present being estimated, and the quantity of 2,5-dimethylfuran adjusted accordingly.

The treatment of the reaction mixtures obtained by the above procedure is described below under the heading of each of the relevant N-nitrosoacetylarylamines.

(i) 4-Methoxy-N-nitrosoacetanilide - A portion (28%) of the reaction mixture was chromatographed on silica (40g.). Elution with benzene gave a white solid (90 mg; m.p. and mixed m.p. 80°) shown to be 4-methoxybiphenyl. The n.m.r. (CCl_4) and i.r. (nujol) spectra compared with those of an authentic sample. Quantitative examination by g11.c. (10% Sil, 152°) using bibenzyl as internal standard gave the yield of 4-methoxybiphenyl (3.5 m/100m). Continued elution of the column with benzene gave a red oil, which, after re-crystallisation from methanol, gave orange crystals (0.19g; m.p. 138°) of 1-(4-methoxyphenyl)-3-acetyl-4-(4-methoxyphenylazo)-5-methylpyrazole (27 m/100m). Found: C,65.6; H, 5.5; N, 14.8; M^+364. $C_{20}H_{20}N_4O_3$ requires C, 65.9; H, 5.5; N, 15.4%; M^+364. N.m.r. ($CDCl_3$): τ , 7.83 (s, 3H, Acetyl); 7.3, (s, 3H Me); 6.18 (s,6H, 2Meo); 2-3.1 (two A2B2 systems superimposed, 8H, aromatic), i.r.(nujol) 1696 cm^{-1} C=O. The Oxime of the compound had m.p. 197.5°. Found: C,63.4; H, 5.3; N.18.1; M^+379. $C_{20}H_{21}N_5O_3$ requires C, 63.4;

H, 5.5; N, 18.4% M^+ 379. N.m.r. ($CDCl_3$): τ , 7.61 (s, 3H, oxime Me); 7.23 (s, 3H, pyrazole Me); 6.07 (s, 6H, 2MeO); 2-3.1 (complex, 9H, phenyl and oxime protons). I.r. (Nujol) showed the absence of the carbonyl absorption at 1696 cm^{-1}.

(ii) 3-Methoxy-N-nitrosoacetanilide - A portion (35%) of the reaction mixture was chromatographed on silica (50g). Elution with petroleum gave a colourless oil (85 mg) found to be 3-methoxybiphenyl. N.m.r. ($CDCl_3$): τ , 6.23 (s, 3H, MeO); 2.4-3.4 (complex, 9H aromatic). Continued elution with petroleum gave a second colourless oil (49 mg) found to be 2-(3-methoxybenzyl)-5-methylfuran. Found: C, 77.6; H, 7.3 $C_{13}H_{14}O_2$ requires C, 77.3; H, 6.9% N.m.r. (CCl_4): τ , 7.78 (s, 3H, Me); 6.27 (s, 3H, MeO); 6.19 (s, 2H, CH_2); 4.15 (s, 2H, furan H_3 and H_4); 2.6-3.5 (complex, 4H, Ph). The aromatic absorption pattern was compared with those of 2-, 3- and 4-methoxytoluenes. The spectrum proved comparable with that of 3-methoxytoluene thus confirming the structure of the product (15% of the 1- and 4- isomers would have been detected). Continued elution of the column gave a tar (0.4g) which proved to be intractable.

Quantitative examination of the reaction mixture by g.l.c. (2% NPGS, 144°) with dibenzyl as internal standard gave 3-methoxybiphenyl (6 m/100m) and 2-(3-methoxybenzyl)-5-methylfuran (19 m/100m).

(iii) 4-Carbethoxy-N-nitrosoacetanilide - A portion (72%) of the reaction mixture was chromatographed on silica (100g). Elution with petroleum/benzene (1:0 - 5:1) gave white crystals (55 mg) of 4-carbethoxybiphenyl (m.p. 46° lit m.p.[147] 46°). N.m.r. (CCl_4) τ , 8.4 (t, 3H, CH_3); 5.5 (q, 2H, CH_2); 1.6-2.6 (complex, 9H, aromatic). Continued elution gave a second colourless oil (40 mg) shown to be 2-(4-carbethoxybenzyl)-5-methylfuran. Found: C, 73.6; H, 7.1. $C_{15}H_{16}O_3$ requires C, 73.7; H, 6.5%. N.m.r. (CCl_4): τ , 8.65 (t, 3H, CH_3); 5.7 (q,2H, CH_2); 7.78 (s, 3H, ring CH_3); 6.11 (s, 2H, CH_2); 4.24 (s, 2H, furan H_3 and H_4); 1.8-2.0 (A_2B_2, 4H, aromatic). Elution of the column with diethyl ether afforded a red oil which on recrystallisation from methanol/petroleum (1:1) yielded yellow crystals (m.p. 91-93°) of 1-(4-carbethoxyphenyl)-3-acetyl-4-(4-carbethoxyphenylazo)-5-methylpyrazole (0.26g 15 m/100m). Found: C,64.2; H, 5.4; N, 12.4; M^+448. $C_{24}H_{24}N_4O_5$ requires C, 64.3, H, 5.3; N, 12.5%; M^+448. N.m.r. ($CDCl_3$): τ , 8.58 (t, 6H, 2Me), 5.5 (q, 4H, $2CH_2$); 7.35 (s, 3H, acetyl); 7.2 (s, 3H, pyrazole Me); 1.6-2.5 (complex, 8H, aromatic). I.r. (nujol) absorptions at 1680-1720 cm^{-1} C=O.

Quantitative examination of the reaction mixture by g.l.c. (2% APL, 186°) using bibenzyl as internal standard gave the yields 4-carbethoxybiphenyl (11.3 m/100m) and 2-(4-carbethoxybenzyl)-5-methylfuran (7.1 m/100m).

(iv) 3-Carbethoxy-N-nitrosoacetanilide - A portion (83%) of the reaction mixture was chromatographed on silica (100g). Elution with petroleum/benzene (40:1) increasing to (10:1) gave a colourless oil (0.35g) which on g.l.c. examination (2% APL, 190°) proved to be a mixture of two compounds. Further elution of the column with chloroform yielded a red oil which, on low temperature recrystallisation from benzene/petroleum (1:10) gave low-melting crystals, melting to a red oil which was found to be 1-(3-carbethoxyphenyl)-3-acetyl-4-(3-carbethoxyphenylazo)-5-methylpyrazole. (0.78g, 27 m/100m). Found: C, 64.5; H, 5.4; N, 12.3. $C_{24}H_{24}N_4O_5$ requires C, 64.3; H, 5.4; N, 12.5%. N.m.r. ($CDCl_3$): τ , 8.6 (t, 6H, 2Me); 5.55 (q, 4H, $2CH_2$); 7.4 (s, 3H, acetyl); 7.3 (s, 3H, pyrazole Me); 1.5-2.7 (complex, 4H, aromatic). I.r. (film) absorptions at 1680-1720 cm^{-1} C=O. Preparative g.l.c. (10% Sil, 172°) of the oil obtained initially from the column afforded 3-carbethoxybiphenyl as a colourless oil: N.m.r. (CCl_4): τ , 8.6 (t, 3H, Me); 5.6 (q, 2H, CH_2); 1.75-2.8 (complex, 9H, aromatic): and 2-(3-carbethoxybenzyl)--5-methylfuran as a colourless oil. Found: C, 74.0; H, 6.75. $C_{15}H_{16}O_3$ requires C, 73.7; H, 6.5%. N.m.r. (CCl_4): τ , 8.62 (t, 3H, Me); 5.65 (q, 2H, CH_2); 7.79 (s, 3H, furan Me); 6.1 (s, 2H, CH_2); 4.13 (s, 2H, CH_2); 4.13 (s, 2H, furan H_3 and H_4); 2.0-2.3 and 2.5-2.8 (complex, 4H, aromatic). I.r. (film) 1720 cm^{-1}, C=O. Quantitative g.l.c. examination of the reaction

mixture (2% APL, 206.5°) using dibenzyl as internal marker gave 3-carbethoxybiphenyl (4 m/100m) and 2-(3-carbethoxybenzyl)-5-methylfuran (8.6 m/100m).

(V) 4-Methyl-N-nitrosoacetanilide - A portion of the reaction mixture was chromatographed on silica (90g). Elution with petroleum gave white crystals of 4-methylbiphenyl (92 mg, m.p. and mixed m.p. 49°) whose i.r. (film) and n.m.r. (CCl_4) spectra were indistinguishable from those of an authentic sample. Elution of the column with diethyl ether gave a red oil which, on recrystallisation from petroleum, gave red crystals (0.53g, 20 m/100m) of 1-(4-methylphenyl)-3-acetyl-4-(4-methylphenylazo)-5-methylpyrazole (m.p. 105°). Found; C, 72.4; H, 6.0; N, 16.6. $C_{20}H_{20}N_4O$ requires C,72.3; H, 6.0; N, 16.9%. N.m.r. ($CDCl_3$): τ , 7.58 (s, 6H, $2ArCH_3$); 7.49 (s, 3H, acetyl); 7.33 (s, 3H, pyrazole Me); 2.2-3.0 (complex, 8H, aromatic). I.r. (nujol): 1685 cm^{-1} (C=O). Quantitative g.l.c. examination (2% APL, 150°) of the reaction mixture with naphthalene as internal standard showed the presence of 4-methylbiphenyl (3.2 m/100m).

(6) 3-Methyl-N-nitrosoacetanilide - A portion (80%) of the reaction mixture was chromatographed on silica (90g). Elution with petroleum gave a colourless oil (0.31g) which on g.l.c. examination (2% APL, 160°) proved to be a mixture of two components. Elution with diethyl ether gave a red oil, which was washed with sodium bicarbonate solution and water and dried over magnesium

sulphate. The resulting red oil (1.94g) resisted all attempts at identification. Found: C, 73.2; H, 6.5; N, 14.3%.

Preparative g.l.c. (10% Sil, 150°) of the colourless oil obtained initially afforded a pure sample of 3-methylbiphenyl (n.m.r. (CCl_4) and i.r. (film) spectra were indistinguishable from those of an authentic sample), and of 2-(3-methylbenzyl)-5-methylfuran. Found: C, 83.9; H, 7.5. $C_{13}H_{14}O$ requires C, 84.1; H, 7.4%. N.m.r. ($CDCl_3$); τ , 7.84 (s, 3H, furan CH_3); 7.75 (s, 3H, $ArCH_3$); 6.24 (s, 2H, CH_2); 4.3 (s, 2H, furan H_3 and H_4); 3.07 (broad, 4H, Ph). Comparison of the aromatic absorption in the n.m.r. spectrum with those of 2- and 3- xylenes again confirmed the presence of the 3-isomer.

Quantitative g.l.c. (10% Sil, 143°) using biphenyl as internal stanard showed the presence of 3-methylbiphenyl (6.5 m/100m) and 2-(3-methylbenzyl)-5-methylfuran (9 m/100m).

9 REACTIONS OF SOME SOURCES OF PHENYL RADICALS AND BENZYNE WITH OTHER SUBSTITUTED FURANS.

a 2-Methylfuran.

(i) Dibenzoyl peroxide - A solution of dibenzoyl peroxide (7.26g, 30 mmol) in 2-methylfuran (4.9g, 60 mmol) and benzene (28g, 0.36 mol) was boiled under reflux for 36h. A portion of the reaction mixture (80%) when cooled, yielded white crystals. Recrystallisation of these crystals from benzene afforded a sample of benzoic

acid (1.2g, m.p. and mixed m.p. 122°) whose i.r.(nujol) spectrum was indistinguishable from that of an authentic sample. The reaction mixture remaining after the removal of the benzoic acid was washed with sodium bicarbonate and water, and dried over magnesium sulphate. The solvent was evaporated yielding a yellow oil of which 0.5g was chromatographed on silica (40g), eluting with petroleum containing an increasing proportion of benzene. Two compounds were obtained as colourless oils the first being identified as : 2-benzoyloxy-5-methylfuran (0.13g) Found: C, 71.1; H, 5.2; M^+ 202. $C_{12}H_{10}O_3$ requires C, 71.3; H, 4.95% M^+ 202. N.m.r. (CCl_4): τ , 7.76 (s, 3H, Me); 4.0-4.2 (complex, 2H, furan H_3 and H_4); 1.7-2.0 (complex, 2H) and 2.4-2.6 (complex, 3H, phenyl). I.r. (film) 1750 cm^{-1}, carbonyl. The second compound was identified as 2-benzoyloxymethylfuran (0.2g) Found: C, 72.2; H, 5.5m M^+ 202. Calc. for $C_{12}H_{10}O_3$: C, 71.3; H, 4.95%, M^+ 202. N.m.r. (CCl_4): τ , 4.74 (s, 2H, CH_2); 2.45-2.7 (complex, 2H furan H_4, and H_3); 1.8-2.1 (complex, 2H) and 2.4-2.8 (complex, 4H, phenyl and furan H_5), i.r. (film) 1720 cm^{-1}, carbonyl.

Examination of the reaction mixture by g.l.c. (1½% CAR, 125.5°) using biphenyl as internal standard showed the presence of 2-benzoyloxy-5-methylfuran (11.3 m/100m) and 2-benzoyloxymethylfuran (13.5 m/100m). Treatment of the remainder of the reaction mixture with sodium bicarbonate followed by acidification and contin-

uous extraction of the aqueous layer gave a sample of benzoic acid (1.12g, 99 m/100m).

(ii) N-Nitrosoacetanilide - N-Nitrosoacetanilide (2.5 g, 15.25 mmol) was allowed to decompose overnight in a mixture of 2-methylfuran (2.46g, 30.0 mmol), and benzene (14g, 0.18 mol) under anhydrous conditions and an atmosphere of oxygen-free nitrogen. The solution was then boiled gently under reflux for 1h. Distillation of the bulk of the reaction mixture gave a yellow oil (0.25g, b.p. 90-120°/0.5 mm) which on examination by g.l.c. (2% APL, 120°c; 2% NPGS, 110°) proved to be a mixture of biphenyl and an unknown compound. Preparative g.l.c. (10% NPGS, 175°) afforded pure samples of biphenyl (m.p. and mixed m.p. 71°, i.r. (film) spectrum indistinquishable from that of an authentic sample), and 2-methyl-5-phenylfuran whose n.m.r. (CCl_4) and i.r. (film) spectra were indistinguishable from those of an authentic sample.

Quantitative examination of the reaction mixture by g.l.c. (10% APL, 170°) using bibenzyl as internal standard gave: biphenyl 4.8 m/100m and 2-methyl-5-phenylfuran (7.6 m/100m).

b Decomposition of N-Nitrosoacetanilide in 2,5-Di-t-butylfuran

N-Nitrosoacetanilide (4.97g, 30 mmol) was allowed to decompose at room temperature overnight in a mixture of 2,5-di-t-butylfuran (10.8g, 60 mmol) and benzene (28g, 0.36 mol). The solution was boiled under reflux

for 1h, and a portion (62%) was distilled, giving a dark oil b.p. 140-160°/12.0 mm (0.5g) which was chromatographed on silica (60g), eluting with petroleum. Biphenyl (0.3g) was obtained m.p. and mixed m.p. 70° i.r. (film) spectrum was indistinguishable from that of and authentic sample. A pale yellow oil (55 mg) was also obtained, identified as 2,5-di-t-butyl-3-phenylfuran. Found: C, 84.7; H, 9.1; M^+ 256. Calc. for $C_{18}H_{24}O$: C, 84.5; H, 9.4; M^+ 256. N.m.r. ($CDCl_3$): τ , 8.78 (s, 18H Bu^t), 2.56-3.2 (complex, 6H, aromatic). Examination of the reaction mixture by g.l.c. (10% Sil, 170.5°) with anthracene as internal standard gave, biphenyl (12.5 m/100m) and 2,5-di-t-butyl-3-phenylfuran (11 m/100m).

c Decomposition of N-Nitrosoacetanilide in 1,2,3,4-Tetramethylfuran

N-Nitrosoacetanilide (3.34g, 20.2 mmol) was allowed to decompose overnight at room temperature in a mixture of 1,2,3,4-tetramethylfuran (4.98g, 40.2 mmol) and benzene (18.8 g, 0.24 mol). The mixture was then boiled under reflux for 1h, and a portion of the reaction mixture (86%) was chromatographed on silica (80g) eluting with a mixture of petrcleum/benzene, 1:50. Biphenyl (55mg) was collected, m.p. and mixed m.p. 71°, i.r. (film) indistinguishable from that of an authentic sample, followed by a colourless oil (0.1g) which proved to be a mixture of 2-benzyl-3,4,5-trimethylfuran and 3-benzyl-2,4,5-trimethylfuran. Found: C, 83.75; H, 8.3.

$C_8H_{12}O$ requires C, 84.0; H, 8.0% N.m.r. ($CDCl_3$): τ 8.4 (s, 2- and 5- Me); 8.1 (s, 3- and 4- Me); 6.43 (s, 2- CH_2); 6.64 (s, 3-CH_2); 3.1 (s, aromatic). Quantitative examination of the reaction mixture by g.l.c. (10% Sil, 143°) using anthracene as internal marker gave the combined yields of the 2- and 3- isomers to be 31 m/100m. Examination by g.l.c. (2% APL, 133°) showed furthermore that the ratio of the 2-isomer to the 3- isomer was 8.6:1.

d N-Nitrosoacetanilide in 2,5-Dimethyl-3,4-dicarbethoxyfuran

N-Nitrosoacetanilide (1.72g, 10.5 mmol) was allowed to decompose at room temperature overnight in a mixture of 2,5-dimethyl-3,4-dicarbethoxyfuran (5g. 21 mmol), and benzene (9.8g, 0.125 mol). The mixture was boiled under reflux for 1h, and the reaction mixture distilled to give, after removal of the solvent, a dark red oil (1.0g, b.p. 90-110°/0.1-0.05 mm). N.m.r. ($CDCl_3$) analysis of the oil showed no absorption corresponding to a methylene attached to the furan nucleus, but it was considered that the ethyl methylene absorption might lie on top of that of the furan methylene and obliterate it. Thus, a portion (0.8g) of the mixture was boiled with potassium hydroxide (0.5g) in a mixture of methanol/water (1:1) (12ml) for 3h. After cooling the reaction mixture, water (50ml) was added, and the aqueous layer was extracted with ether (20ml). The aqueous layer was acidified with hydrochloric acid and a reddish oil (0.28g) separated. The n.m.r. ($CDCl_3$) spectrum of this oil again did

not show an absorption corresponding to a methylene group attached to a furan nucleus (2 m/100m)of a compound containing this group would have been detected).

10 REACTION OF PENTYL NITRITE WITH ARYLAMINES IN THE PRESENCE OF ARYNE TRAPS

It was found that when a mixture of aniline, pentyl nitrite, acetic anhydride, potassium acetate, acetic acid, and the aryne trap 2,3,4,5- tetraphenylcyclopentadienone (tetracyclone) in benzene was boiled, one of the reaction products was the benzyne adduct 1,2,3,4-tetraphenylnaphthalene (TPN). Blank experiments showed that this was formed neither by a mixture of acetic anhydride, aniline,and tetracyclone nor by a mixture of pentyl nitrite,and tetracyclone.

The reaction mixtures were worked up by chromatography on alumina, eluting first with petroleum until biphenyl had been eluted, and then with petroleum/benzene (9:1) until the TPN had been eluted. The biphenyl and TPN were collected and weighed, their purity being checked by comparison of the i.r. (nujol) spectrum with those of standard samples, by melting point, and by mixed melting point. A sample of TPN was recrystallised from acetic acid and analysed,found: C, 94.3; H, 5.75. Calc. for $C_{34}H_{24}$: C, 94.4; H, 5.6%.

a Conditions for the Maximum Yield of 1,2,3,4-Tetraphenylnaphthalene from 2,3,4,5-Tetraphenylcyclopentadienone and Aniline.

(i) Table 3 - The quantities of each reactant and

Table 3 Reaction of Pentyl Nitrite with Aniline and Acetic Anhydride

Reactants										
Aniline (mmol)	10	10	10	10	10	10	10	10	10	10
Pentyl Nitrite (mmol)	10	10	10	15	15	15	15	15	15	15
Acetic Anhydride (mmol)	20	20	30	30	30	30	30	30	30	30
Acetic Acid (ml)	0.1	0.1	0.1	0.1	-	-	-	-	-	-
Tetracyclone (mmol)	10	10	10	10	20	20	20	20	20	20
Potassium Acetate (mmol)	10	10	10	10	15	10	-	-	-	-
Yield of Biphenyl (m/100m)	15.2	8.2	15.5	11.5	12.2	8.6	10.2	8.3	8.0	31.0
Yield of TPN (m/100m)	14.5	4.9	12.2	13.7	16.6	29.8	23.7	31.7	21.0	9.0
Method employed	A	B	A	C	D	E	A	E	F	G

The yields of biphenyl and TPN (m/100m based on aniline) are to be found in Table 3. The particular experimental method employed in each case is described in the notes given below, under the relevant key letter.

A The reactants were mixed and boiled under reflux in benzene (30ml) for 24h.

B The amine, dissolved in benzene (10ml) was added dropwise to a mixture of the other reactants in boiling benzene. The reaction mixture was boiled under reflux for a further 24h.

C The reactants were mixed and stirred in benzene (30ml) at 60° for 24h.

D Pentyl nitrite, dissolved in benzene (10ml) was added to the rest of the reactants which had been stirred in benzene (20ml) at 60° for 30 min. Stirring was continued at 60° for a further 24h.

E Pentyl nitrite, dissolved in benzene (10ml), was added dropwise over 5h to a mixture of the other reactants in boiling benzene (20ml). The mixture was boiled under reflux for a further 24h.

F Solutions of pentyl nitrite and aniline in benzene (5ml each) were dripped simultaneously into a mixture of the other reactants in boiling benzene (20ml). The mixture was boiled under reflux for a further 24h.

G High dilution: The conditions were as for E, but the volumes of benzene were increased tenfold.

ii Table 4 - Pentyl nitrite (0.88g, 7.5 mmol) in benzene (5ml) was added dropwise over a specified period

(Addition Time - Table 4) to a mixture of aniline (0.5g, 5.4 mmol), tetracyclone (1.92g, 10 mmol), and acetic anhydride (1.5g, 14.7 mmol) in refluxing benzene (10ml). The reaction mixture was then boiled under reflux for a further period of time (Reflux Time - Table 4). The yields of TPN (m/100m based on aniline)are also given in the table.

Table 4. The Effect of Varying Time Periods on the Yield of TPN from Pentyl Nitrite/Aniline/Acetic Anhydride.

Addition Time (h)	5	3	1
Reflux Time h	24	24	2.5
Yield of TPN (m/100m)	27.3	27.0	25.

b Solvent Effects on the Yield of 1,2,3,4-Tetraphenylnaphthalene from 2,3,4,5-Tetraphenylcyclopentadienone and Aniline.

Pentyl nitrite (0.9g, 7.7 mmol) in the solvent (5ml) was added dropwise over 1 h to a mixture of tetracyclone (1.92g, 10 mmol), acetic anhydride (1.5g,14.7 mmol) and aniline (0.5g, 5.4 mmol) in the boiling solvent. Boiling was continued under reflux for 24h. Solvents used were

(i) 1,2-Dimethoxyethane - Yield of TPN 20 m/100m
(ii) Cyclohexane - Yield of TPN, 17 m/100m
(iii) Benzene - Yield of TPN 27 m/100m

c Reaction Using Preformed Acetanilide

Pentyl nitrite (0.9g, 7.7 mmol) in benzene (5ml) was added dropwise over 5h to a mixture of acetanilide

(0.67g, 5 mmol), tetracyclone (1.9g, 10 mmol) in boiling benzene (i) with acetic anhydride (1.5g, 14.7 mmol) (ii) without acetic anhydride. The reaction mixture was boiled under reflux for 24h. TPN was isolated (i) in 21 m/100m yield (the corresponding yield from aniline was 32 m/100m) and (ii) 7 m/100m.

d Reactions Using Other Dehydrating Agents

Pentyl Nitrite (0.9g, 7.5 mmol) in benzene (5ml) was added dropwise over 1h to a mixture of aniline (0.5g, 5.4 mmol), tetracyclone (1.92g, 10 mmol), and the dehydrating agent (15 mmol) in boiling benzene (10ml). The reaction was boiled under reflux for 24h. Results are expressed below in Table 5.

Table 5. Use of Other Dehydrating Agents.

Dehydrating Agent	Yield of TPN(m/100m)
Acetyl Chloride	20
Phosphorous Pentoxide	0
4-Chlorobenzoic Anhydride	39

e Other Benzyne Traps.

(i) Anthracene - Pentyl nitrite (1.75g, 15 mmol) in benzene (5ml) was added dropwise over 5h to a mixture of aniline (1g, 10 mmol), potassium acetate (1g, 10 mmol), acetic anhydride (3.06g, 30 mmol) and anthracene (5.4g, 20 mmol) in boiling benzene. The mixture was boiled under reflux for a further 24h, the solvent was evaporated, and the residue was boiled under reflux with maleic anhydride (2g) in chlorobenzene (15ml) for 1h. Chromatography of a portion of the reaction mixture on alumina (40g) eluting

with benzene afforded a sample of triptycene (0.1g) m.p. and mixed m.p. 256°. The i.r. (nujol) spectrum was indistinguishable from that of an authentic sample of triptycene. Examination of the reaction mixture by g.l.c. (2% NPGS, 204°; 1% SE30, 158°) with fluoranthene as internal standard showed the presence of triptycene (10 m/100m).

(ii) 2,5-Di-p-methylphenyl-3,4-diphenylcyclopentadienone- Pentyl nitrite (0.59g, 5 mmol), aniline (0.46g, 5 mmol), 2,5-di-p-methylphenyl-3,4-diphenylcyclopentadienone (1.03g, 5 mmol), potassium acetate (0.5g, 5 mmol), acetic acid (0.05ml), and acetic anhydride (1.53g, 15 mmol) were boiled under reflux in benzene (15ml) for 24h. The reaction mixture was chromatographed on alumina as described in the case of TPN giving 1,4-di-p-methylphenyl-2,3-diphenylnaphthalene (0.35g, 15 m/100m) m.p. and mixed m.p. 225.5°. The i.r. (nujol) spectrum was indistinguishable from that of an authentic sample of 1,4-di-p-methylphenyl-2,3-diphenylnaphthalene.

f Other Arylamines with 2,3,4,5-Tetraphenylcyclopentadienone.

Pentyl nitrite (0.9g, 7.7 mmol) in benzene (5ml) was added dropwise over 1h to a mixture of the arylamine (5 mmol), acetic anhydride (1.5g, 14.7 mmol), and tetracyclone (1.9g, 10 mmol) in boiling benzene. The reaction mixture was boiled under reflux for 24h, and chromatographed on alumina in the manner described earlier for TPN. The following results were obtained.

(i) From 3-chloroaniline obtained 1,2,3,4-tetraphenyl-5-chloronaphthalene (18 m/100m) m.p. 242°. Found: C, 87.6; H, 4.9. $C_{34}H_{23}Cl$ requires C, 87.4; H, 4.9%

(ii) From 3-bromoaniline obtained 1,2,3,4-tetraphenyl-5-bromonaphthalene (21 m/100m) m.p. 228-230° (lit[143] m.p.= 235°). Found: C, 79.7; H, 4.3. Calc. for $C_{34}H_{23}Br$: C, 79.8; H, 4.5%.

(iii) From 3-anisidine obtained a mixture of 1,2,3,4-tetraphenyl-5-methoxynaphthalene and 1,2,3,4-tetraphenyl-6-methoxynaphthalene (29 m/100m) m.p. 216°. I.r. (nujol) spectrum compared with that of an authentic sample of the two isomers. Found: C, 90.9; H, 5.8. Calc. for $C_{35}H_{26}O$: C, 90.8; H, 5.7%.

(iv) From 3-toluidine obtained a mixture of 1,2,3,4-tetraphenyl-5-methylnaphthalene and 1,2,3,4-tetraphenyl-6-methylnaphthalene (25.5 m/100m) m.p. 217°. I.r.(nujol) spectrum compared with that of an authentic mixture of the two isomers. Found: C, 94.2; H, 6.2. Calc. for $C_{35}H_{26}$: C, 94.1; H, 5.9%.

(v) From 4-toluidine obtained 1,2,3,4-tetraphenyl-6-methylnaphthalene (4 m/100m) m.p. 223° (lit[21] m.p. 224°). Found : C, 94.2; H, 6.2. Calc. for $C_{35}H_{26}$: C,94.1; H, 5.9%. The i.r. (nujol) spectrum was indistinguishable from that of an authentic sample.

11 REACTION OF ARYL NITRITES WITH ANILINE AND ITS DERIVATIVES IN THE PRESENCE OF BENZYNE TRAPS

In the following reactions 1,2,3,4-tetraphenylnaphthalene was isolated using dry column techniques (see p.40). The dry columns were made up from alumina (80g) in both glass and nylon tubing (diameter 1½"), the position of the TPN band being determined by its fluorescence under u.v. light (350 nm). The columns were developed with cyclohexane. The purity of the biphenyl and TPN isolated was checked by comparison of their i.r.(nujol) spectra with those of authentic samples, by melting point (lit biphenyl[147] 70°, lit[150] TPN 204-204.5°), and by mixed melting point.

a Benzoyl Nitrite and Aniline.

Benzoyl nitrite (2g, 13 mmol) in benzene (5ml) was added dropwise over 1h to a mixture of aniline (0.5g, 5.4 mmol), and tetracyclone (1.9g, 10 mmol) in boiling benzene. The mixture was boiled under reflux for 12h and then maleic anhydride (1g) was added, and boiling was continued until the colour due to tetracyclone had gone. Dry column chromatography of this reaction mixture gave biphenyl (6 m/100m) and TPN (9 m/100m).

b 4-Chlorobenzoyl Nitrite and Aniline

(i) With acetic anhydride - 4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (5ml) was added dropwise to a mixture of aniline (0.5g, 5.4 mmol), acetic anhydride (1.5g, 14 mmol) and tetracyclone (1.92g, 10 mmol) in boiling benzene (10ml). The reaction mixture was boiled under reflux overnight and, having added maleic anhydride (1g), was boiled until the colour from tetracyclone had gone. Dry column chromatography gave TPN (0.82g, 38.0 m/100m)

and biphenyl (0.07g, 9 m/100m).

(ii) With 4-chlorobenzoic anhydride - Aniline (0.5g, 5.4 mmol), 4-chlorobenzoic anhydride (4.35g, 15 mmol), and tetracyclone (1.92g, 10 mmol) were boiled under reflux in benzene (10ml) for 30 min. 4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (5ml) was added dropwise over 1h and the mixture was boiled under reflux for 12h. Maleic anhydride (1g) was added and the mixture was boiled until the colour of tetracyclone had gone. Dry column chromatography gave TPN (0.96g, 45 m/100m) and biphenyl (0.16g, 21 m/100m).

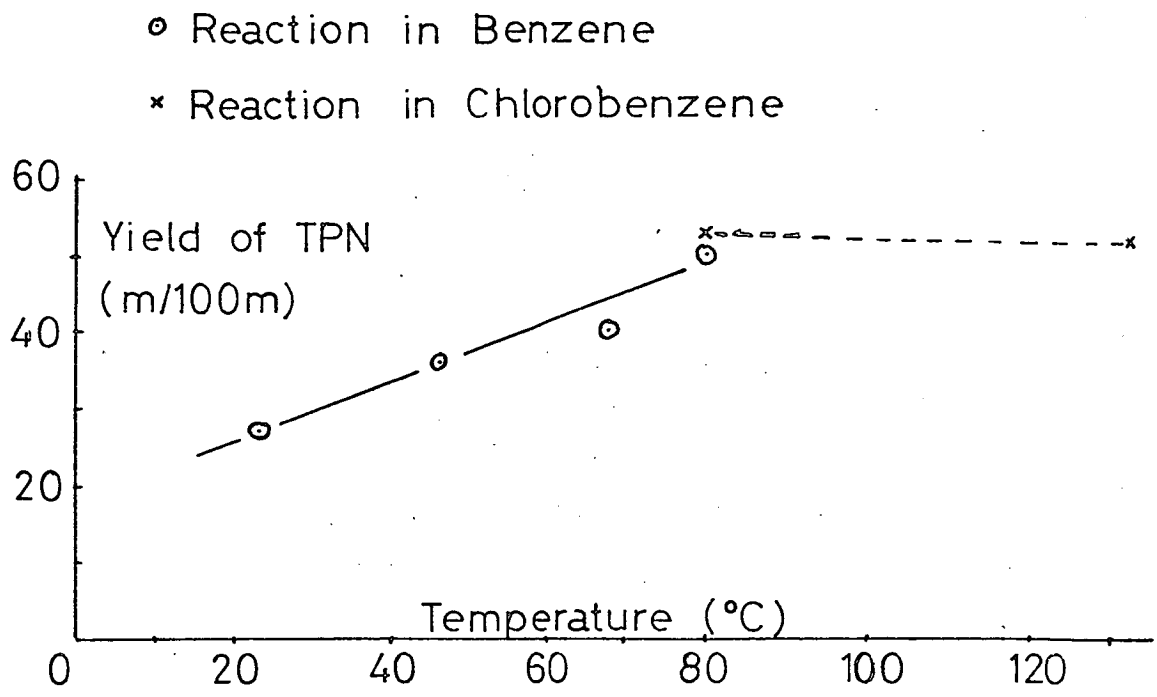
c 4-Chlorobenzoyl Nitrite and 4-Chlorobenzanilide

4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (5ml) was added dropwise over 1h to a mixture of 4-chlorobenzanilide (1.15g, 5 mmol), and tetracyclone (1.9g, 10 mmol) in boiling benzene (10ml). The mixture was boiled under reflux overnight, and then boiled with maleic anhydride (1g) to remove the excess tetracyclone. Dry column chromatography gave TPN (1.02g, 48 m/100m) and biphenyl (0.06g, 8 m/100m).

d 4-Chlorobenzoyl Nitrite and Acetanilide

4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (5ml) was added dropwise over 1h to a mixture of acetanilide (0.67g, 5 mmol), and tetracyclone (1.9g, 10 mmol), in boiling benzene (10ml) and the reaction mixture was boiled under reflux for 12h. Treatment with maleic anhydride followed by dry column chromatography as described before gave TPN (1.1g, 51 m/100m) and biphenyl (0.08g, 10 m/100m).

GRAPH I : The Effect of Temperature on the yield of TPN, from 4-Chlorobenzoyl Nitrite/ acetanilide/Tetracyclone



(ii) The effect of temperature - The reaction as described above was conducted at temperature ranging from room temperature to the boiling point of benzene. In addition, two reactions were conducted using chlorobenzene as solvent, one at 80° and the other at its boiling point. The results obtained are expressed graphically in Graph 1.

(iii) The effect of the 4-chlorobenzoyloxy anion- The reaction as described above (i) was carried out in the presence of sodium 4-chlorobenzoate (0.9g, 5 mmol). Chromatography gave TPN (0.66g, 31 m/100m) and biphenyl (0.03g, 4 m/100m).

e High Dilution Reactions of 4-Chlorobenzoyl Nitrite and Acetanilide with Benzyne Traps

(i) Tetracyclone - 4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (50ml) was added over 1h to a mixture of acetanilide (0.675g, 5 mmol) and tetracyclone (1.9g, 10 mmol) in boiling benzene (100 ml). The mixture was boiled under reflux for 12 h and then the mixture was concentrated. The work up was as described in the previous section (c) giving TPN (1.5g, 70 m/100m) and biphenyl (0.06g, 8 m/100m).

(ii) Anthracene-4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (50ml) was added over 1h to a boiling solution of acetanilide (0.675g, 5 mmol), and anthracene (0.9g, 5 mmol) in benzene (100ml). The reaction mixture was boiled under reflux for 12h and then concentrated. Maleic anhydride (1g) was added and the solution was boiled for 3h. Chromatography of a portion of the reaction mixture on alumina (60g) eluting with benzene, gave white crystals (0.1g) of triptycene which

were recrystallised from petrol. M.p. and mixed m.p. 256° i.r. (nujol) spectrum was indistinguishable from that of an authentic sample. G.l.c. (2% NPGS, 214°) analysis with fluoranthene as internal standard gave the yield of trypticene to be 16 m/100m.

(iii) 9,10-Dimethoxyanthracene -4-Chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (50ml) was added over 1h to a solution of acetanilide (0.675g, 5 mmol), and 9,10-dimethoxyanthracene in boiling benzene 100ml. The mixture was boiled under reflux for 12h and the solvent was replaced by chlorobenzene (20ml). Maleic anhydride (1g) was added to the mixture which was boiled for 1h. Chromatography of a portion of the mixture on alumina (60g) eluting with petrol/benzene 3:1 gave white crystals (0.12g) of 9,10-dimethoxytriptycene m.p. and mixed m.p. 192° i.r. (nujol) spectrum was indistinguishable from that of an authentic sample. G.l.c. (2% NPGS,214°) examination using triptycene as marker gave the yield of 9,10-dimethoxytriptycene to be 14 m/100m.

(iv) Methyl methacrylate - To a boiling solution of acetanilide (0.675g, 5 mmol) in methyl methacrylate (2.28g, 20 mmol) and benzene (100ml) a solution of 4-chlorobenzoyl nitrite (1.6g, 8.5 mmol) in benzene (50ml) was added dropwise over a period of 1h. The reaction mixture was boiled under reflux overnight and the bulk was chromatographed on alumina (60g) eluting with petroleum until biphenyl (60mg, m.p. and mixed m.p. 70°) had been eluted. Elution with petroleum/ether 19:1 gave

an impure oil (0.2g) which, on preparative g.l.c. (2% CAR, 109°), afforded a pure sample of 2-carbmethoxy-3-phenylprop-1-ene. I.r. (film) and n.m.r. ($CDCl_3$) spectra compared with those reported in the literature. Found: C, 75.3; H, 7.1. Calc. for $C_{11}H_{12}O_2$: C, 75.0; H, 6.8%. Quantitative examination of the reaction mixture by g.l.c. (2% CAR 115°) using naphthalene as internal standard gave the yields biphenyl (8.5 m/100m) and 2-carbmethoxy-3-phenylprop-1-ene (31. m/100m).

12 COMPETITION REACTIONS OF 4-CHLOROBENZOYL NITRITE AND ACETANILIDE

a Anthracene and 9,10-Dimethoxyanthracene - 4-Chlorobenzoyl nitrite (0.8g, 4.3 mmol) in benzene (25ml) was added dropwise over 1h to a boiling solution of acetanilide (0.387g, 2.9 mmol), anthracene (1.78g, 11.5 mmol), and 9,10-dimethoxyanthracene (2.38g, 11.5 mmol) in benzene (50ml). The reaction mixture was boiled under reflux for 12h, and then chromatographed on alumina (50g) eluting with a mixture of ether and petrol ether, 1:1. The fluorescent band was collected and analysed by g.l.c. (2% NPGS, 214°) to give the competition ratio $K_H^{OMe} = 2.85$.

b 1,4-Dimethoxyanthracene-4-Chlorobenzoyl nitrite (0.8g, 4.3 mmol) in benzene (25ml) was added dropwise over 1h to a boiling solution of acetanilide (0.39g, 3 mmol), and 1,4-dimethoxyanthracene (1.19g, 5.5 mmol) in benzene (50ml). The reaction mixture was boiled under reflux and examined by g.l.c. (10% Sil Oil, 225°; 2% NPGS 214°). The competition constant between "A" and "B" rings was found to be $K_A^B = 3.2$.

13 MISCELLANEOUS REACTIONS

a N-Nitrosoacetanilide with Diethyl Ether

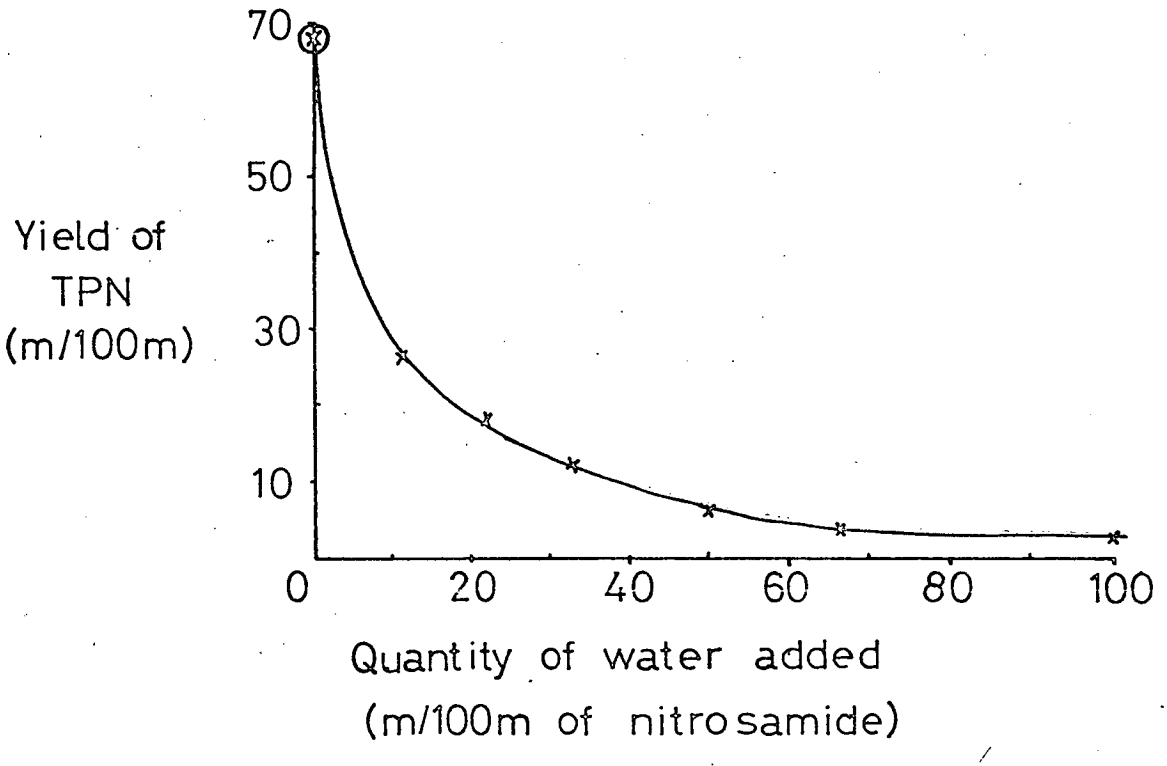
N-Nitrosoacetanilide (4.97g, 30 mmol) was allowed to decompose in a mixture of diethyl ether (4.44g, 60 mmol) and benzene (28.1g, 0.36 mol) for 12h. The reaction mixture was then heated slowly to the boiling point and boiled under reflux for 1h. G.l.c. examination of reaction mixture (2% NPGS, 127°) showed no peak that could be assigned to 1-ethoxy-1-phenylethane.

b Benzyne Sources with 2,3,4,5-tetraphenylcyclopentadienone in the presence of water.

(i) Benzenediazonium fluoroborate - To a mixture of tetracyclone (1.92g, 5 mmol), potassium acetate (1g, 12 mmol), acetic acid (0.1 ml), and water (0.18g, 10 mmol) in benzene (30ml), benzenediazonium fluoroborate (1.92g, 10 mmol) was added in three batches, with 30 min between each addition. The temperature of the reaction mixture was maintained at 60°. The mixture was stirred at 60° for 1h and chromatographed on alumina (70g), eluting with a mixture of petrol ether and benzene (10:1). 1,2,3,4-tetraphenylnaphthalene (0.1375g, 3.2 m/100m) was obtained which recrystallised from acetic acid, m.p. and mixed m.p. 200°, i.r. (nujol) spectrum was indistinguishable from that of an authentic sample of 1,2,3,4-tetraphenylnaphthalene. A similar experiment in the absence of water had given 1,2,3,4-tetraphenylnaphthalene (1.3g, 30 m/100m)

(ii) N-nitrosoacetanilide - N-Nitrosoacetanilide (0.82g, 5 mmol) was allowed to decompose in a solution of

GRAPH II : The Effect of Water on the Yield of TPN from N-Nitrosoacetanilide/Tefracyclone



⊗ This result was obtained by Mr. A. Robertson

tetracyclone (1.92g, 5 mmol) in benzene (10ml) containing amounts of water ranging from 0.09g (5 mmol) to zero. The reaction mixtures were stirred at room temperature for 12h and then boiled under reflux for 1h, and maleic anhydride (1g) was added, and the reaction mixtures boiled under reflux until the tetracyclone colour had gone. Chromatography on alumina dry columns (70g), eluting with cyclohexane, gave almost constant yields of biphenyl (4 m/100m) but yields of tetraphenyl naphthalene which are detailed in graph 2. It was found that amyl alchohol had a similar repressant effect upon the yield of 1,2,3,4-tetraphenylnaphthalene but that acetic acid had no effect on the yield of 1,2,3,4-tetraphenylnaphthalene in parallel experiments.

c N-Nitrosoacetanilide with 2,5-Dimethylthiophene

N-Nitrosoacetanilide (4.97g, 30.3 mmol) was allowed to decompose in a solution of 2,5-dimethylthiophene (6.72g, 60 mmol) in benzene (28.1g, 0.36 mol) overnight at room temperature, under anhydrous conditions, and an atmosphere of oxygen-free nitrogen. The reaction mixture was boiled under reflux for 1h, the solvent was evaporated from a major part of the reaction mixture. The remaining dark oil (2.6g) was distilled to give an oil (0.5g) b.p. 60-100° / 0.2 mm which proved on g.l.c. examination (2% APL 140°) to be a mixture of two compounds. Preparative g.l.c. afforded pure samples of biphenyl (m.p. and mixed m.p. 71°, i.r. (film) spectrum indistinguishable from an authentic sample of biphenyl), and 2,5-dimethyl-3-phenylthiophene

n.m.r. (CCl_4), and i.r. (film) spectra were indistinguishable from those of an authentic sample of 2,5-dimethyl-3-phenylthiophene. Quantitative examination by g.l.c., (10% APL, 170°) using naphthalene as internal standard gave biphenyl (12 m/100m) and 2,5-dimethyl-3-phenylthiophene (3 m/100m). The residue (2g) from the distillation of the reaction mixture was extracted into chloroform and taken from the flask. All attempts to work up this oil failed.

d Reactions of Aryldiazonium Chloride Solutions with 2,5-dimethylfuran in the Presence of Potassium Acetate.

The method of the reaction was that described by Eastman and Detert[151] who added, all at once, the diazonium salt solution obtained from the arylamine (50 mmol) sodium nitrite (3.5g), 10% hydrochloric acid (30ml), and water (150ml), to an ice-cold mixture of 2,5-dimethylfuran (4.8g, 50 mmol), potassium acetate (15g, 0.25 mol) and ethanol (250ml). The mixture was kept at 0° for 3h and then thrown into twice its volume of water. A red oil separated which was extracted into benzene, and the extract dried over magnesium sulphate:-

(ii) Benzenediazonium Chloride (from Aniline) - The benzene solution obtained in the above manner was chromatographed on silica (70g) eluting with ether/benzene 1:4. A red oil identified as 1-phenyl-3-acetyl-5-methylpyrazole (5.4g, 54 m/100m) was obtained. N.m.r.($CDCl_3$): τ, 7.71 (s, 3H, acetyl); 7.42 (s, 3H Me); 3.31 (s, 1H, pyrazole ring proton); 2.55 (s, 5H, pH), i.r. (film) 1680cm^{-1} C=O.

The oxime of this compound was prepared m.p. 151°, i.r. (film) showed the loss of the carbonyl frequency at 1680 cm^{-1}. N.m.r. ($CDCl_3$): τ, 7.66 (s, 3H, oxime Me); 7.62 (s, 3H, pyrazole ring Me); 3.43 (s, pyrazole ring proton) 2.56 (s, 5H, Ph); 1.94 (broad, 1H oxime proton). Found: C, 67.2; H, 5.9; N, 19.9; M^+ 215. $C_{12}H_{13}N_3O$ requires C,67.0; H, 6.05; N, 19.5%; M^+ 215.

Examination of the original benzene extract by g.l.c. (2% APL, 140°) showed that 2-benzyl-5-methylfuran was absent (0.2% would have been detected).

(11) 4-Methoxybenzenediazonium chloride (from 4-Anisidine) - The dry benzene extract obtained in the above fashion was chromatographed on silica (80g), eluting with benzene/ether, 9:1. A red oil (5.1g) was obtained which on recrystallisation from ethanol/water 20:1 gave dark red crystals m.p. 84° identified as 1-(4-methoxyphenyl)-3-acetyl-5-methylpyrazole (3.1g, 27 m/100m) n.m.r. ($CDCl_3$): τ, 7.72 (s, 3H acetyl); 7.51 (s, 3H, ring Me); 6.15 (s, 3H, MeO); 3.31 (s, 1H, pyrazole ring proton); 2.5-3.1 (A_2B_2, 4H, Ph); i.r. (nujol) 1675 cm^{-1} (carbonyl). Found: C, 68.0; H, 5.9; N, 12.0; M^+ 230. $C_{13}H_{14}N_2O_2$ requires C, 67.8; H, 6.1; N, 12.2% M^+ 230).

e 3-Methoxyacetanilide with 4-Chlorobenzoyl Nitrite in Methyl Methacrylate

4-Chlorobenzoyl Nitrite (3.2g, 17 mmol) in benzene (100 ml) was added dropwise over 1h to a boiling solution of 3-methoxyacetanilide (1.67g, 10 mmol), and methyl methacrylate (4.56g, 45 mmol) in benzene (200ml. The bulk of the reaction mixture was chromatographed on

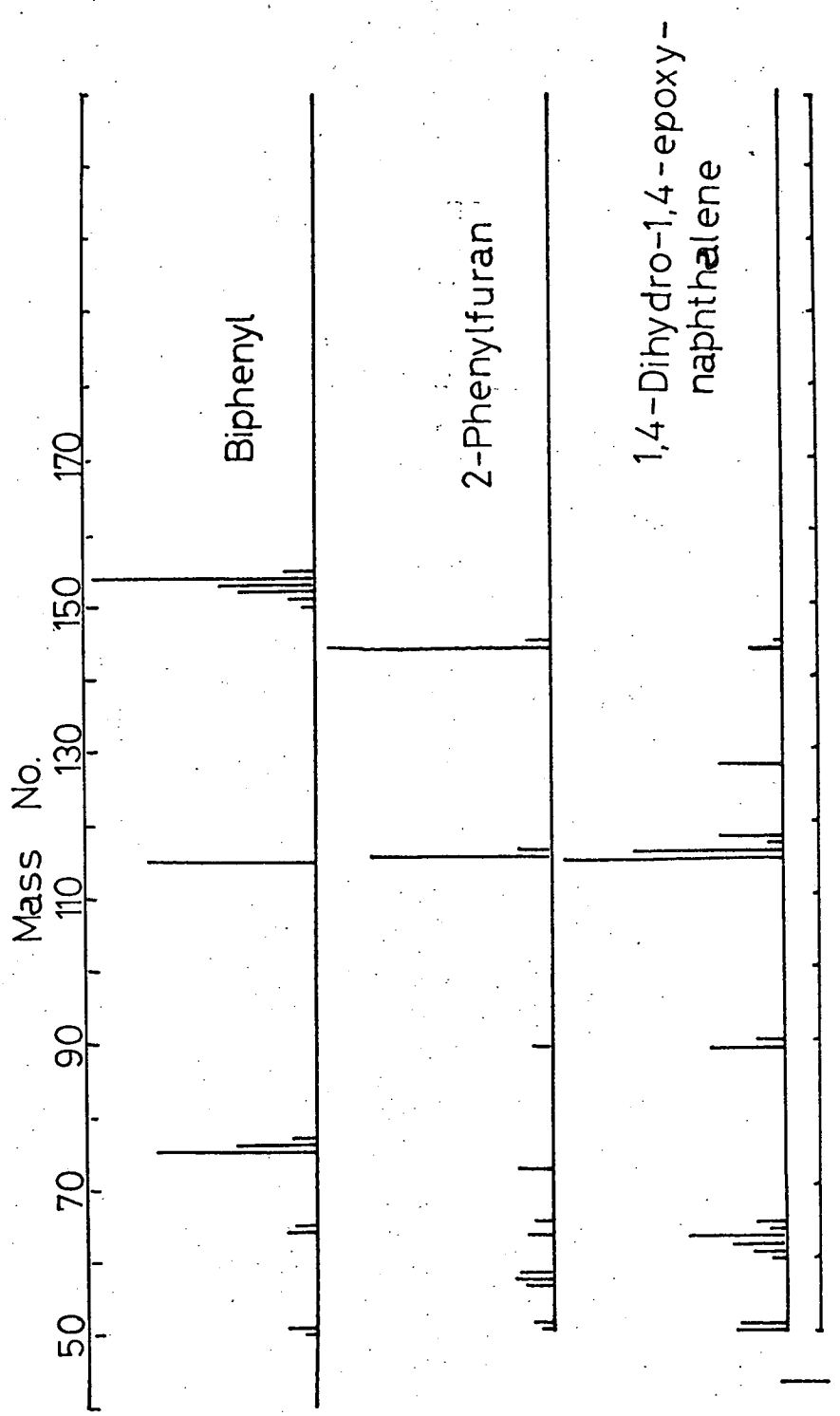
alumina (90g), eluting initially with petrol, and finally with petrol/ether 1:1. A colourless oil was obtained whose n.m.r. ($CDCl_3$) and i.r. (film) spectra were identical to that of 3-methoxybiphenyl. (0.1g, 6 m/100m) and a second colourless oil which was found to be 2-carbmethoxy-3-(3-methoxyphenyl)prop-1-ene. (0.5g, 25 m/100m) n.m.r. ($CDCl_3$): τ, 6.3, (s, 3H, Me); 6.25 (s, 3H, MeO); 6.42 (broad s, 2H, CH_2); 4.56 (complex, 1H) and 3.8 (complex, 1H) ethylenic protons; 2.8 and 3.2 (complex, 4H, aryl). Found: C, 69.8; H, 6.6; M^+, 206. $C_{12}H_{14}O_3$ requires C, 69.9; H, 6.8%; M^+ 206.

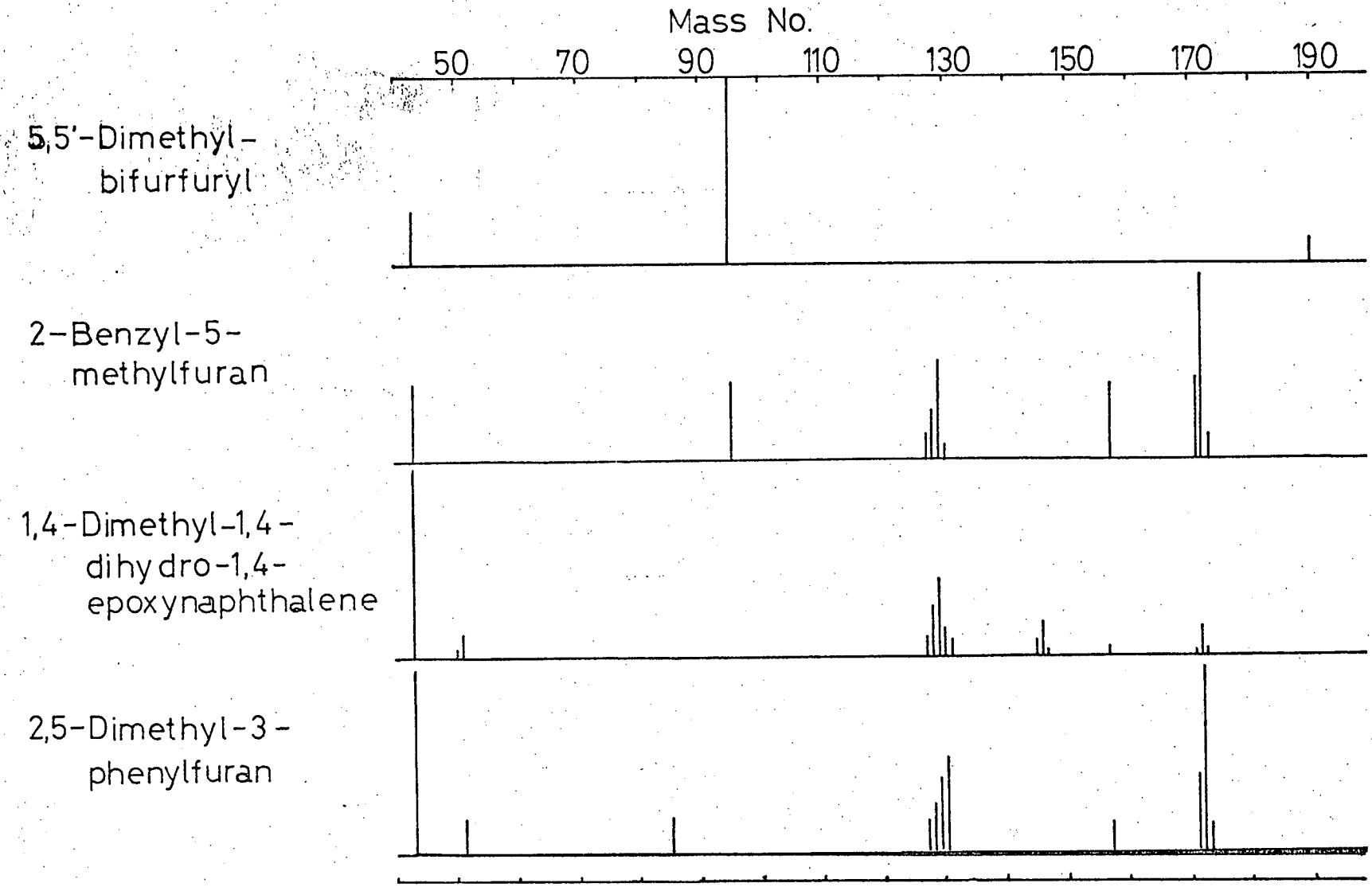
An examination of the n.m.r. spectrum of this compound, and those of 3- and 4- methoxytoluenes showed that 20% of the 4-methoxy isomers would have been detected in the product, i.e. the product consisted of the 3-methoxy-isomer in over 80% proportion.

f Reaction of 1-(4-Methoxyphenyl)-3-acetyl-5-methylpyrazole with 4-Methoxy-N-nitrosoacetanilide.

4-Methoxy-N-nitrosoacetanilide (1g) was added to a solution of 1-(4-methoxyphenyl)-3-acetyl-5-methylpyrazole (1g) in benzene (10ml) and the reaction mixture was stirred under anhydrous conditions and an atmosphere of oxygen-free nitrogen overnight. The reaction mixture was then boiled for 1h. T.l.c. examination of the reaction mixture on alumina showed the presence of unchanged 1-(4-methoxyphenyl)-3-acetyl-5-methylpyrazole (R_F=0.46) but no 1-(4-methoxyphenyl)-3-acetyl-4-(4-methoxyphenylazo)-5-methylpyrazole (R_F=0.27) was detected.

APPENDIX I : MASS SPECTRAL DATA




Mass No.
50
70
90
110
130
150
170
190
5,5'-Dimethyl-bifurfuryl
2-Benzyl-5-methylfuran
1,4-Dimethyl-1,4-dihydro-1,4-epoxynaphthalene
2,5-Dimethyl-3-phenylfuran

DISCUSSION OF RESULTS

PREAMBLE

The decomposition of N-nitrosoacetanilide in furan, and 2,5-dimethylfuran, presented a serious anomaly to the accepted mechanism for the decomposition of acylarylnitrosamines.

In both of these cases, the expected benzyne adducts were not formed, except in minute quantities, and a satisfactory explanation for the formation of the products obtained, 2-phenylfuran, and 2-benzyl-5-methylfuran, had not been postulated.

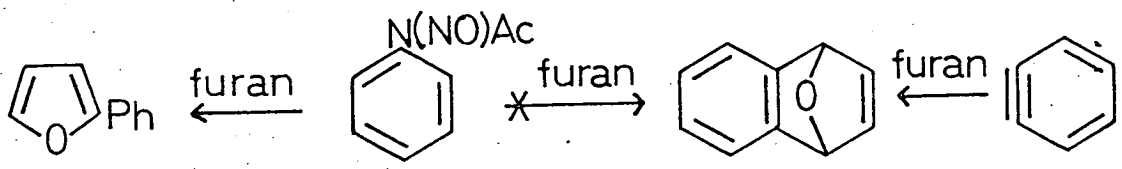
As a result of the research described herein, a satisfactory mechanism for the formation of these compounds has been proposed. Furthermore, knowledge of the mechanism of the decomposition of N-nitrosoacetanilide has lead to two new synthetic routes to arynes, from arylamines, and from acylarylamines.

Throughout this section, 1,2,3,4-tetraphenylnaphthalene will be abbreviated to TPN, and 2,3,4,5-tetraphenylcyclopentadienone to tetracyclone.

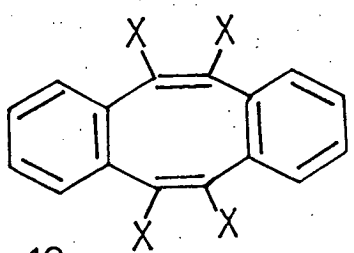
1 THE DECOMPOSITION OF N-NITROSOACETANILIDE IN FURAN.

It was shown by Cadogan et al. that, not only o-t-butyl-N-nitrosoacetanilide[18], but also other acylarylnitrosamines including N-nitrosoacetanilide itself[24], gave 1,2,3,4-tetraphenylnaphthalenes in up to 80% yield on reaction with 2,3,4,5-tetraphenylcyclopentadienones, and triptycenes in up to 30% yield on reaction with anthracenes, thus indicating the intermediacy of arynes. The yield of adduct was found

to be highest when an electron releasing group was present in the arynophile[117]. It was reported, however, that N-nitrosoacetanilide did not form the normal benzyne adduct 1,4-dihydro-1,4-epoxynaphthalene, when reacted with furan, but gave only 2-phenylfuran[114], the expected radical product.



Similarly 2-(4-chlorophenyl)furan arose from the decomposition of 4-chloro-N-nitrosoacetanilide in furan[152].
Cook[117] reported another uncharacteristic reaction of "benzyne" produced by N-nitrosoacetanilide. He observed that when anthranilic acid/pentyl nitrite was used as a source of benzyne in dimethyl acetylenedicarboxylate, the product was 5,6,11,12-tetracarbomethoxy a,e cyclooctatetraene (19), whereas the product from the decomposition of N-nitrosoacetanilide in dimethyl acetylenedicarboxylate was 1,2,3,4-tetracarbomethoxynaphthalene (20, see also scheme 15, p.31).



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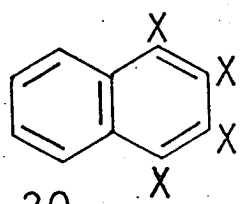
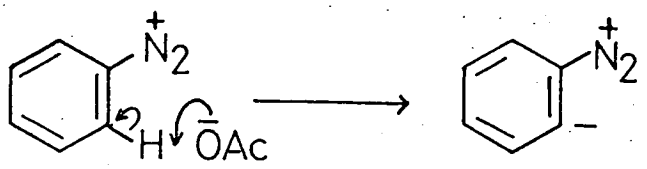


20

Cook[117] explained the anomalous product produced by

N-nitrosoacetanilide in terms of a dipolar benzyne precursor, formed by the removal of an o-proton from the benzenediazonium cation, (scheme 18).



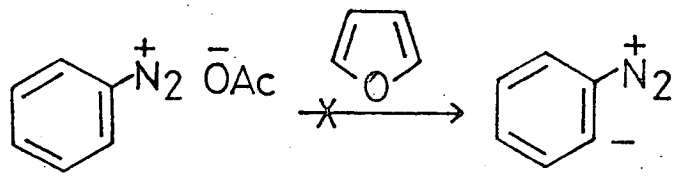
Scheme 18

He argued that the acetate ion was basic enough under anhydrous conditions, to effect the proton removal from the o-position. The results of competitive experiments for N-nitrosoacetanilide, and the authentic benzyne sources, anthranilic acid/pentyl nitrite, and 2-aminobenzotriazole/ lead tetraacetate, gave the same competition constants in each case. Similar decomposition of N-nitrosoacetanilide and of pentyl nitrite/anthranilic acid in a solution of 1,4-dimethoxyanthracene[117], the ratio of "A" to "B" ring adduct was found to be the same from both sources. These results clearly point to the intermediacy of benzyne in these reactions. The abnormal reaction product obtained from the decomposition of N-nitrosoacetanilide in dimethyl acetylenedicarboxylate stems from the reaction of the dipolar benzyne precursor with dimethylacetylene dicarboxylate, before it can decompose to form benzyne.

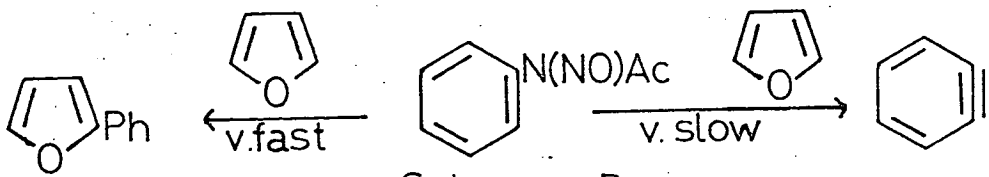
In the case of the decomposition of N-nitrosoacetanilide in furan, the major anomaly was the effective absence of the benzyne-furan adduct (only 0.1 m/100m was detected in this investigation). However, during the course of our invest-

igations, Ruchardt and Tan[153] informed us that they had found the benzyne-furan adduct, in low yields, in the decomposition of benzenediazonium fluoroborate/acetic acid/potassium acetate. We were unable to confirm this result in the case of N-nitrosoacetanilide after repeated experiments, even under very dry conditions, at room temperature. On repetition of the decomposition at the boiling point, however, 5 m/100m of the benzyne-furan adduct was obtained, subsequently found to be identical with the yield obtained in Germany, by Ruchardt and Tan, at the same temperature.

In addition to the effective absence of benzyne-furan adduct in the decomposition of N-nitrosoacetanilide at room temperature in furan, it was also observed that the presence of furan in reaction mixtures was found to suppress the formation of benzyne adduct with other aryne traps[117]. Thus the reaction of N-nitrosoacetanilide with tetracyclone in benzene gave TPN in 22% yield, whereas the same reaction in furan gave only 1.4% of TPN. This suggests that furan is in some way inhibiting the formation of the benzyne/benzynoid species (scheme A), or is removing its precursor before it has a chance to form the intermediate (scheme B). A possible mechanism was considered for each of these alternatives. Formation of a π-complex between furan and benzene might prevent the formation of the benzyne precursor, or a fast redox reaction might be removing it.



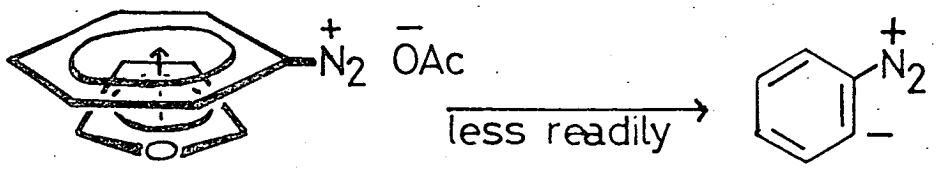
Scheme A



Scheme B

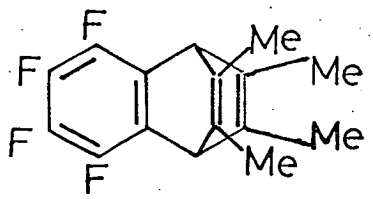
Koller and Zollinger[154] have reported that diazonium salts form π-complexes with naphthalene and 1-methylnaphthalene in dilute acetic acid, and noted that the electrophilicity of the diazonium group was reduced only slightly. Yoshida and Osawa[155] have also reported that furans can act as π-bases, forming complexes with phenol by H-bonding between the phenolic hydrogen and the π-system of the furan. The shift in the O-H absorption in the i.r. spectrum of the complex was reported to show a marked increase when 2,5-dimethylfuran was used in place of furan, which could be expected to be a stronger π-base because of the presence of the two electron donating methyl groups on the nucleus. It might therefore seem reasonable to suggest that the intermediate diazonium ion, formed in the decomposition of N-nitrosoacetanilide, forms a π-complex with furan, thereby reducing the acidity of the o-protons and hence preventing the formation of the benzyne/

benzynoid intermediate.



The alternative method of stabilising the intermediate diazonium ion is by σ-complex formation. This was ruled out by Brydon[114], who isolated TPN in 24% yield from the decomposition of N-nitrosoacetanilide in a solution of tetracyclone in tetrahydrofuran.

Working on the assumption that π-complex formation was indeed occurring, Cook[117] attempted to detect similar suppression of adduct formation in the reaction of N-nitrosoacetanilide with tetracyclone in the presence of electron-rich hexamethylbenzene and durene. Instead of suppression of adduct formation, however, he found that the yields of TPN had been increased by some 10% in each case. Callendar, Coe and Tatlow[156] have shown that the polymethyl aromatic compounds are reactive towards electrophilic arynes by isolating the adduct from the reaction of tetrafluorobenzyne and durene (21). Similarly,



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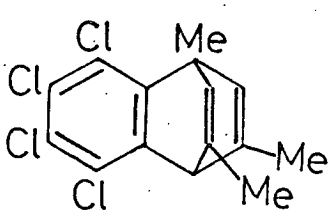


22

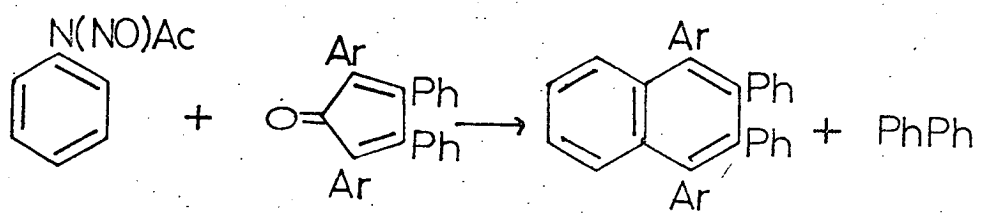
Heany and Jablonski[156] have isolated the adduct formed between tetrachlorobenzyne and mesitylene (22). Cook[117] explained

the increased yields of TPN by suggesting that durene and hexamethylbenzene might be stabilising the intermediate benzyne or benzynoid species, rather than their precursor.

In the reaction of N-nitrosoacetanilide with substituted tetracyclones, it was observed[117] that, as the yields of tetraarylnaphthalene from the reaction rose, the yield of biphenyl dropped (Table 6). This was taken to indicate that the tetraarylnaphthalene had been formed at the expense of the biphenyl, which suggested a common intermediate which could give biphenyl or alternatively, benzyne adduct.

This evidence implies that, in addition to, or instead of, π-stabilisation of the benzenediazonium cation by furan, the phenylation of furan should be much faster than that of benzene, since the benzyne adducts form in benzene, but not in furan.

Table 6 : The Decomposition of N-Nitrosoacetanilide in the Presence of Various Tetracyclones.



Ar =		yields, m/100m	
	Ph	22	16
	4-Me-C_6H_4	82	0
	4-Meo-C_6H_4	82	3
	No Trap	-	43

To test this predication, the rate ratio $K^{furan}_{benzene}$ was determined for a variety of sources of phenyl radicals and/or benzyne. $K^{furan}_{benzene}$ was taken to be the ratio of the yields of 2-phenylfuran and biphenyl obtained when these sources were decomposed in an equimolar mixture of furan and benzene. The results are summarised in Table 7. The most striking feature of the table is that reactions known to involve the intermediacy of the benzenediazonium cation, have extremely high values of $K^{furan}_{benzene}$. Thus our predication that $K^{furan}_{benzene}$ should be large, is correct in the case of N-nitrosoacetanilide. The low value obtained in the case of phenylazotriphenylmethane could have been expected as, under these conditions, addition compounds are also formed in this case[157]. The value of rate ratio obtained for aniline/pentyl nitrite of $K^{furan}_{benzene}$ = 4.8 may be considered to be the competition ratio for the free radical phenylation of furan/benzene. The value of $K^{furan}_{benzene}$ increases for the other sources used (except phenylazotriphenylmethane) up to a maximum value of $K^{furan}_{benzene}$ = 16.5, which was obtained in the case of the decomposition of benzenediazonium fluoroborate/acetic acid/potassium acetate.

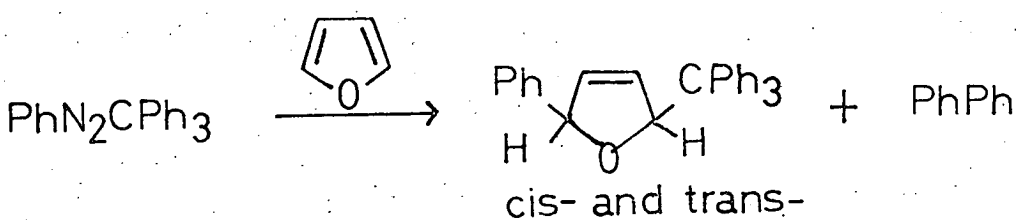


Table 7 : Rate Ratios from Competition Experiments Involving Furan and Benzene with Various Sources of Phenyl Radicals and Benzyne/Benzynoid Species.

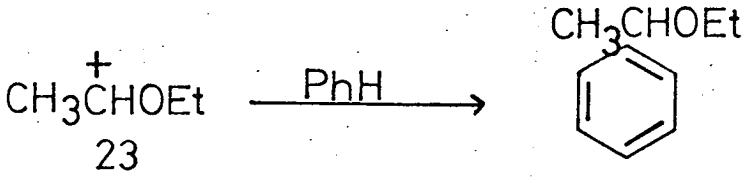
Source Used	Temp. of React.	Rate Ratio $K^{furan}_{benzene}$
NNA	R.T.	15.9
NNA + Water	R.T.	15.9
$PhN_2^+ BF_4$/AcOH/AcOK	57°	16.5
4Cl-C_6H_4 CO_2NO/PhNHAc	b.p.	9.0
$PhNH_2$/AmONO	b.p.	4.8
$PhNH_2$/Ac_2O/AmONO	b.p.	5.4
PAT	b.p.	1.9

PAT = Phenylazotriphenylmethane NNA = N-Nitrosoacetanilide

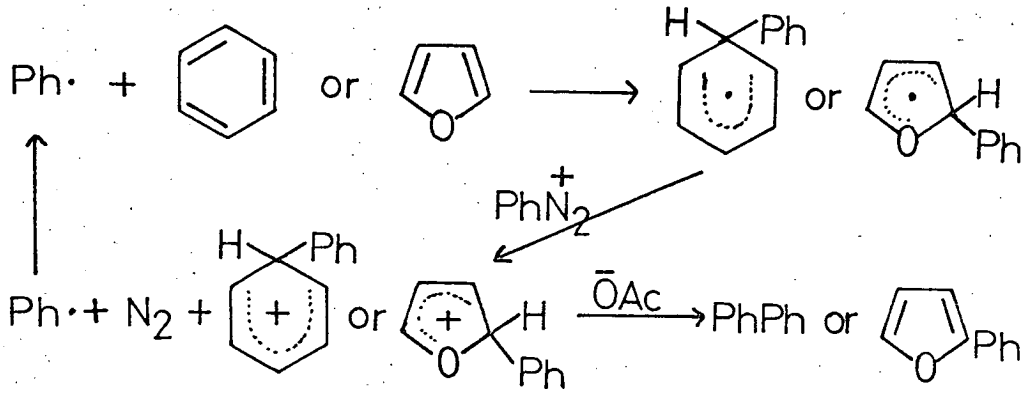
It should be pointed out at this juncture that Tiecco[158] has reported a rate ratio for the decomposition of aniline/pentyl nitrite in furan/benzene of $K^{furan}_{benzene}$ = 11.5. The value recorded above (Table 7) of $K^{furan}_{benzene}$ = 4.8 represents an average value taken of six independent experiments, the spread of results being ± 0.4. The method described by Tiecco was used in some of these rate ratio determinations.

The exceptionally high rate ratios obtained in the case of the decomposition of benzenediazonium fluoroborate/acetic acid/potassium acetate, and of N-nitrosoacetanilide in furan/benzene show that the phenylation of furan is extremely fast in cases where the benzenediazonium cation is known to be present. It was therefore proposed that a redox scheme similar to that proposed[106] for the decomposition of N-nitrosoacetanilide in diethyl ether (scheme 13, p.28) and in benzene (scheme 12 p. 27) might apply in this instance (scheme 19). In an attempt to verify this scheme,

N-nitrosoacetanilide was allowed to decompose in a solution of diethylether in benzene, in the hope that the intermediate carbonium ion (23) might be trapped by the solvent benzene.



No 1-ethoxy-1-phenylethane was discovered in the reaction mixture.



Scheme 19

Scheme 19 invokes the known affinity, of the furan nucleus for electrophilic species. This may lead, not only to π -stabilisation of the diazonium cation, but also a lowering of the activation energy required to reach the transition state for the redox step, which would explain the increase in reaction rate compared to that in benzene, where the analagous stabilisation seems less likely. If this were the case, the preferential removal of the diazonium cation by

this route will lead to the suppression of formation of a benzyne/benzynoid species, and hence of aryne adduct.

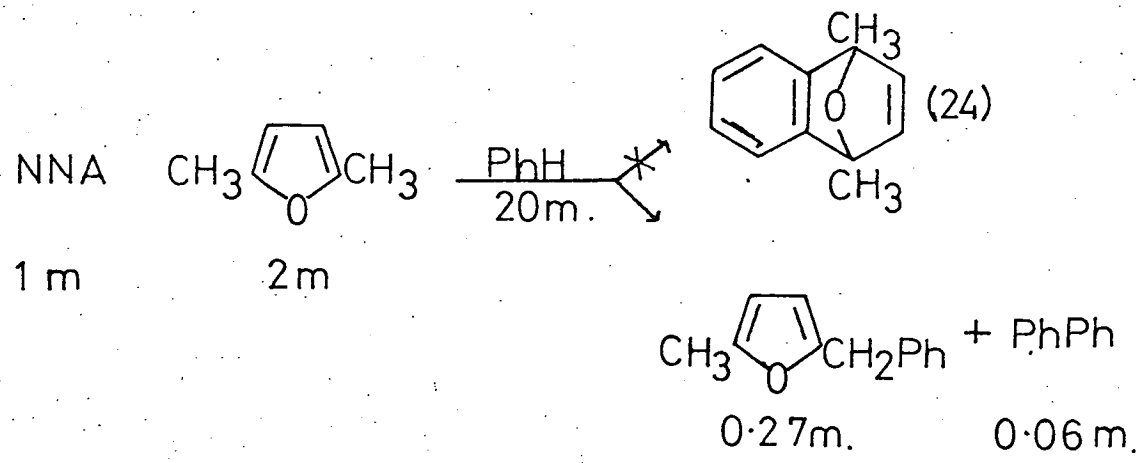
The fact that the yield of benzyne adduct is increased by a factor of fifty when the reaction is conducted at the temperature of boiling furan/benzene mixture suggests, either that, at this temperature, the π-complex is weakened, thus increasing the acidity of the o-proton in the benzenediazonium cation, thereby easing the formation of the benzyne/benzynoid species, or, more probably, that at this temperature the rate of benzyne/benzynoid formation has increased relative to the rate of attack on furan, allowing that these effects may be complementary.

In conclusion, therefore we can now explain the anomaly of the decomposition of N-nitrosoacetanilide in furan since, under certain conditions, the benzyne-furan adduct can be formed, the low yields obtained being in accord with a preferential fast competing radical reaction compared with aryne formation, possibly tempered by a lower proton acidity as a result of π-complex formation.

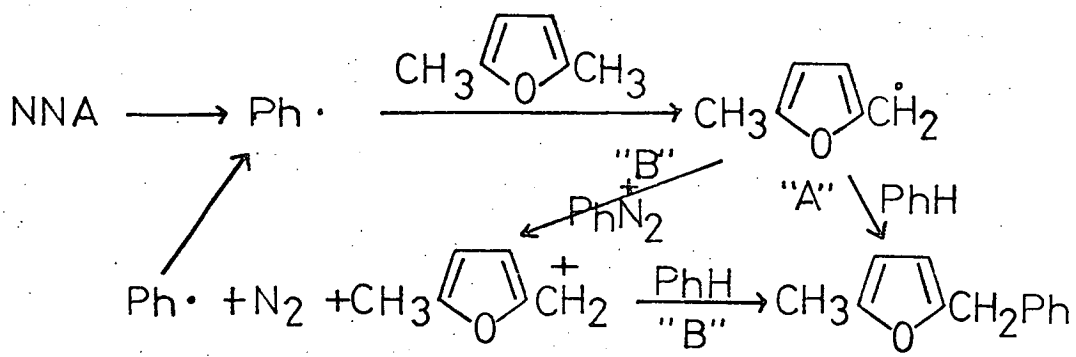
2 THE DECOMPOSITION OF ACYLARYLNITROSAMINES IN 2,5-DIMETHYLFURAN

Noting the report by Brydon[114] that the decomposition of N-nitrosoacetanilide in furan gave 2-phenylfuran, with no adduct formation, Harger[115] attempted a similar reaction using 2,5-dimethylfuran as substrate, expecting that the blocked 2- and 5- positions might force the formation of the benzyne adduct, 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene (24). He found, however, that no benzyne adduct was formed

and that the major products were 2-benzyl-5-methylfuran and biphenyl.



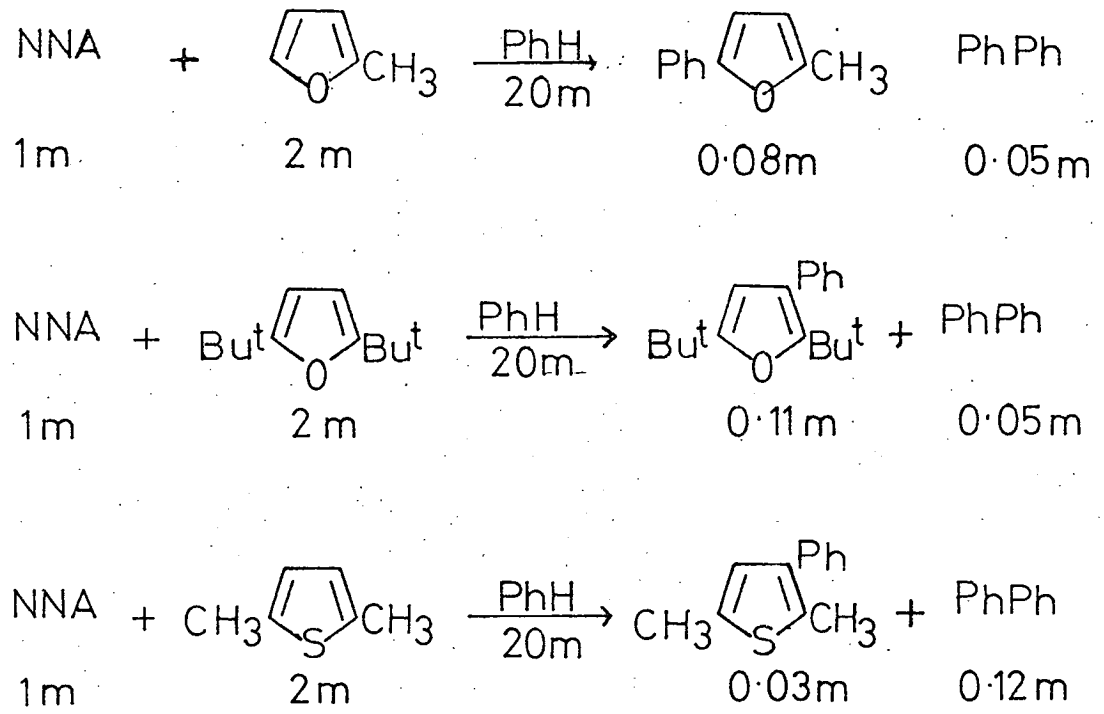
Harger proposed the mechanism shown as pathway A (scheme 20), but no supporting evidence was cited.



Scheme 20

An investigation of the mechanism of this unusual reaction seemed necessary, and the results obtained from the decomposition of N-nitrosoacetanilide in the presence of various substratesare given over, (Table 8).

Table 8 : Reaction of N-Nitrosoacetanilide with Various Substrates



Thus the reaction appeared to be peculiar to 2,5-dimethylfuran. 2,5-Dimethylthiophene, 2-methylfuran, and 2,5-di-t-butylfuran all gave the products expected from radical substitution on systems with blocked 2-, or 2- and 5- positions. Further investigation of the generality of this reaction involving various sources of phenyl radicals and/or benzyne/benzynoid intermediates gave the results summarised in Table 9. As can be seen, 2-benzyl-5-methylfuran is not formed when authentic sources of phenyl radicals are used, the only identifiable product in these cases being biphenyl.

Table 9 : The Reaction of Some Sources of Phenyl Radicals and/or Benzyne/Benzynoid Intermediates with 2,5-Dimethylfuran.

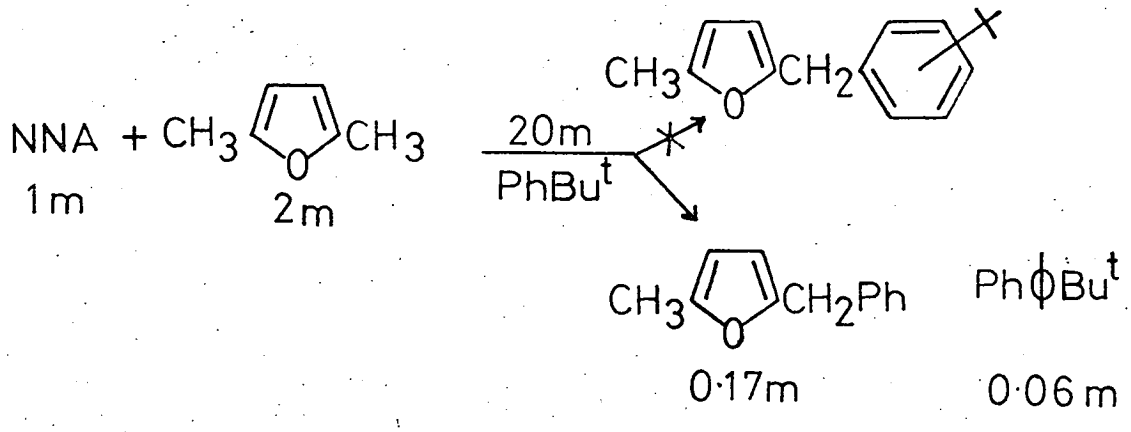
Source	Temp. of React^{n}.	PhPh Yields	B.F.in m/100m	D.M.D.N.
PAT	b.p.	14	0	0
AmONO/$PhNH_2$	b.p.	9	0	0
AmONO/Ac_2O/$PhNH_2$	b.p.	10	0	0
$PhN_2^+ \bar{B}F_4$/AcOH/KOAc	60°	32	2	0
4-Cl-C_6H_4-CO_2NO/PhNHAc	b.p.	64	0	2
NNA	R.T.	6	27	0
NNA + Water	R.T.	3	0.5	0
NNA	b.p.	5	2.4	0.04
NNCB	R.T.	Not Estimated.	30.0	1.0

B.F. = 2-benzyl-5-methylfuran, DMDN = 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene, PAT = phenylazotriphenylmethane, NNA = N-nitrosoacetanilide, NNCB = 4'-chloro-N-nitrosobenzanilide, RT = room temperature.

It can be seen that the reactions which produced 2-benzyl-5-methylfuran were those involving the benzenediazonium cation. Furthermore, increasing the temperature of the reaction or adding water to the system, had a marked effect upon the yield of 2-benzyl-5-methylfuran.

The mechanism proposed by Harger[115] (scheme 20A) was deemed untenable, after the decomposition of N-nitrosoacetanilide in a solution of 2,5-dimethylfuran in t-butylbenzene was found to give 2-benzyl-5-methylfuran, and not 2-(t-butylbenzyl)-5-methylfuran, as would have been re-

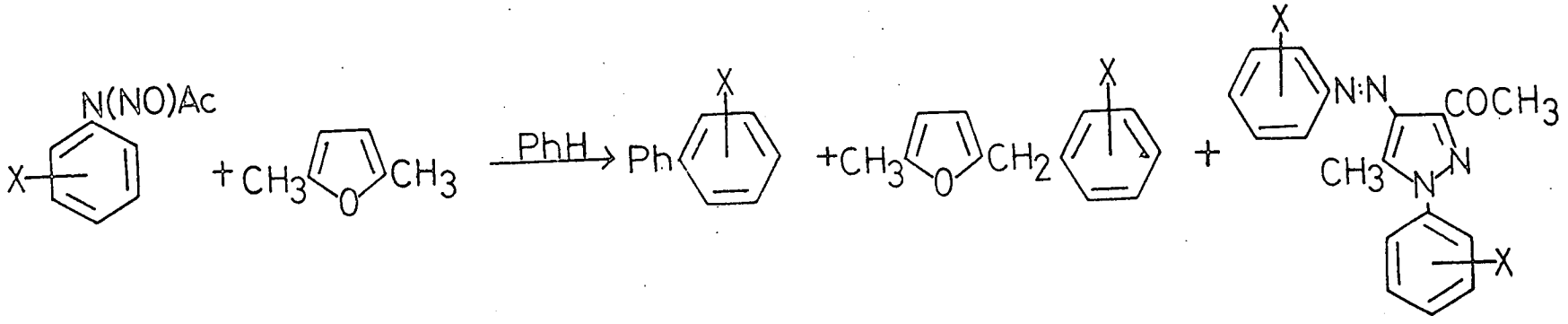
quired by this mechanism.



This result also precludes a mechanism of the type shown in pathway B (scheme 20), as this mechanism also dictates that the cation, formed by the redox reaction with the benzenediazonium cation, should attack the solvent.

A suggestion that 2-benzyl-5-methylfuran might be formed via a benzyne intermediate was discounted when it was shown that the benzyne sources, anthranilic acid/ pentyl nitrite, and 4-chlorobenzoyl nitrite/acetanilide were both found to form the benzyne adduct 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene, no 2-benzyl-5-methylfuran being detected. A control experiment, conducted with 4[1]-chloro-N-nitrosobenzanilide, gave 2-benzyl-5-methylfuran in high yield (30 m/100m), thereby precluding any interference from the 4-chlorobenzoyloxy anion being the reason for the fact that no 2-benzyl-5-methylfuran was detected in the decomposition of 4-chlorobenzoyl nitrite/acetanilide in 2,5-dimethylfuran. A reason for this anomaly is proposed later in the text. Further evidence against the intermediacy of

Table 10 : The Decomposition of Substituted N-Nitrosoacetanilides in 2,5-Dimethylfuran

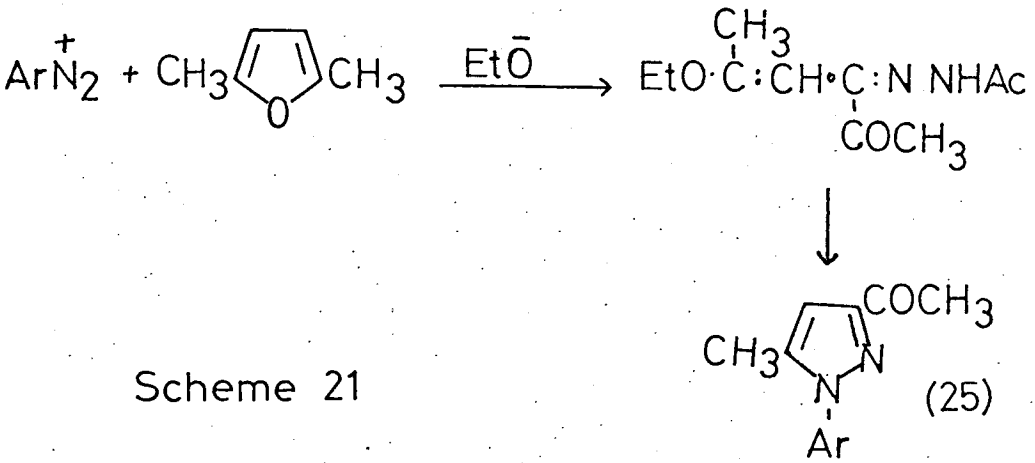


			m/100m
X = H	6	27	*
= 4-MeO	3.5	-	27
= 3-MeO	6	19	
= 4-CO_2Et	11.3	7.1	15
= 3-CO_2Et	4.0	8.6	27
= 4-Me	3.2	-	20
= 3 Me	6.5	9.0	-

* It might be added that the red oil obtained in this case, although unidentified, did have an exact mass corresponding to the formula of the relevant pyrazole.

benzyne, appeared from results of decompositions of substituted N-nitrosoacetanilides in 2,5-dimethylfuran (Table 10). Thus, in the decomposition of 3-methyl-N-nitrosoacetanilide and 3-methoxy-N- nitrosoacetanilide in 2,5-dimethylfuran, only the 3-substituted aryl moiety was found in the products, suggesting a monodentate attack.

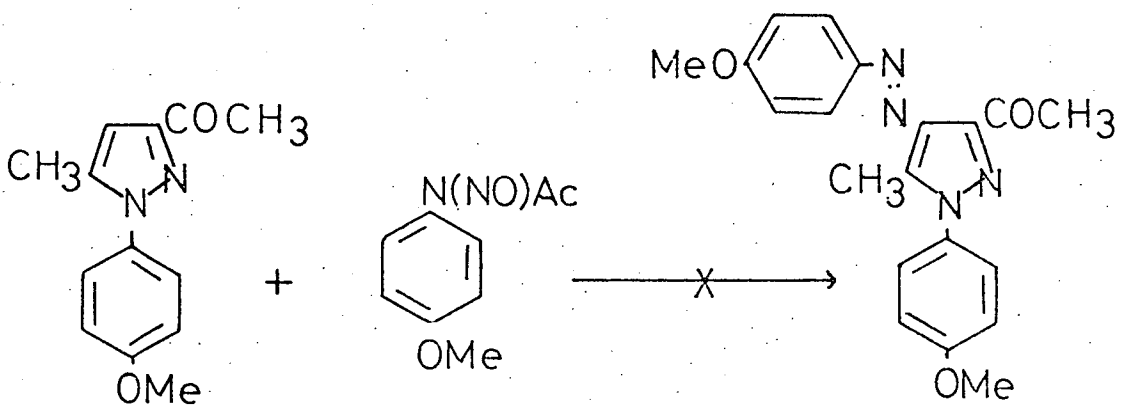
In addition to the benzylfurans, other unexpected products, azo-substituted pyrazoles, were isolated in some of these reactions in yields of up to 27%. The formation of these products relates to a reaction reported by Eastman and Detert[151] in 1948. They reported that the reaction of an aqueous solution of 4-nitrobenzenediazonium chloride with an ethanolic solution of 2,5-dimethylfuran, in the presence of potassium acetate at 0°, gave a red oil when the reaction mixture was quenched in an excess of water. Heating this red oil in vacuo gave 1-(4-nitrophenyl)-3-acetyl-5-methylpyrazole (25) Eastman and Detert proposed a mechanism of the type shown in Scheme 21.



Scheme 21

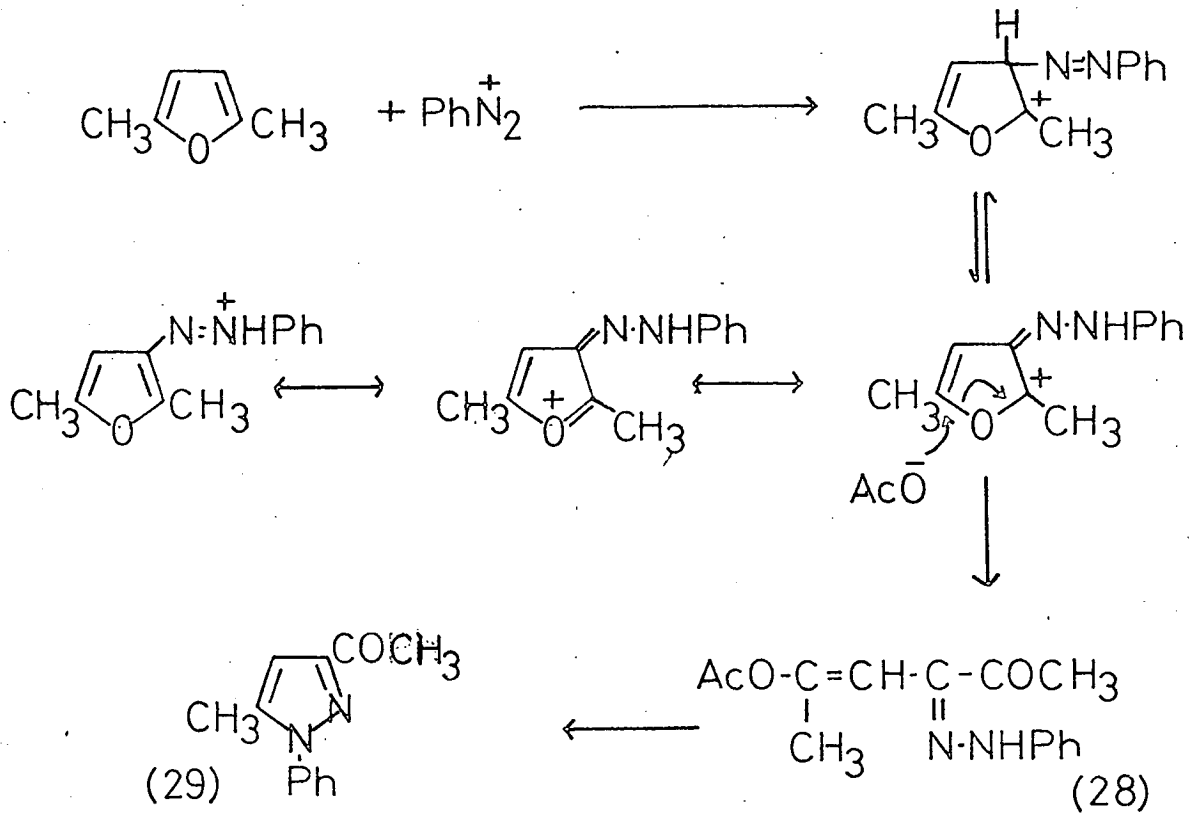
(25)

In an attempt to explain the substituted pyrazoles obtained from the decomposition of acylarylnitrosamines in 2,5-dimethylfuran (Table 10), it was considered that, under the reaction conditions, the pyrazole (25) might undergo electrophilic substitution at position 4. Consequently, 4-methoxy-N-nitrosoacetanilide was allowed to decompose in a solution of 1-(4-methoxyphenyl)-3-acetyl-5-methylpyrazole (26) to test the validity of this statement (scheme 22). No 1-(4-methoxyphenyl)-3-acetyl-4-(4-methoxyphenylazo)-5-methylpyrazole (27) was detected in the reaction mixture which discounted this possible mechanism.

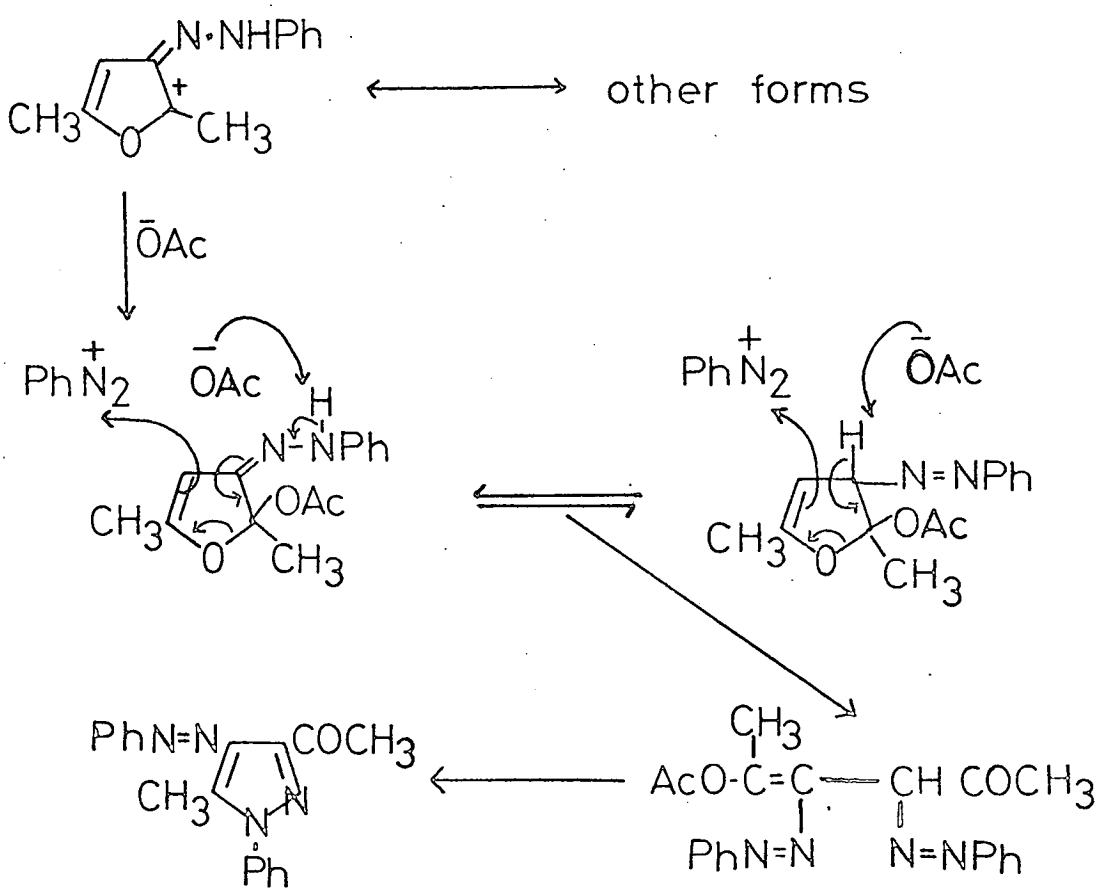


(26) Scheme 22 (27)

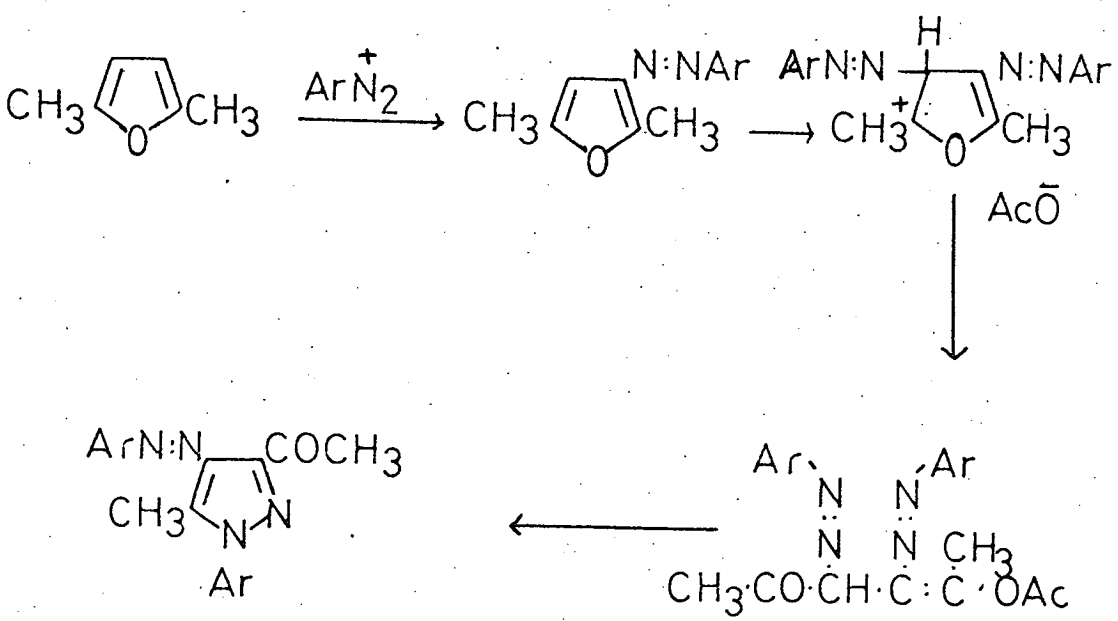
An alternative scheme was considered in which 2,5-dimethylfuran underwent a coupling reaction at position 3 followed by addition at position 4 and ring-opening (scheme 23). The scheme was thought to be improbable, however, there being no obvious reason why a second azo-group should add to the 4-position of the furan ring, as this would be deactivated by the azo- group in 3-position.



Scheme 24



Scheme 25

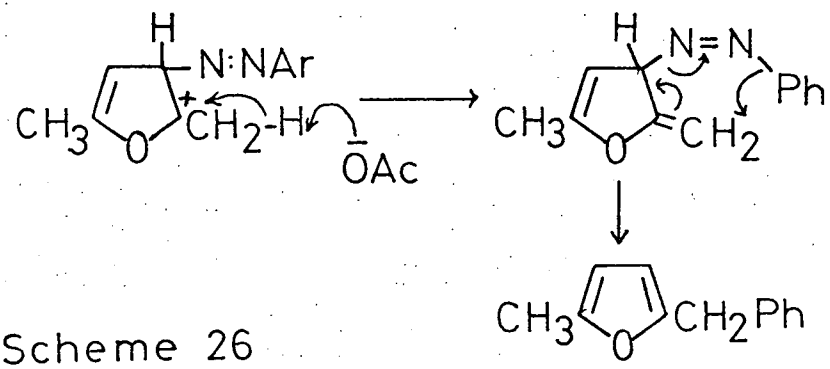


Scheme 23

A more acceptable explanation invokes the tautomeric formation of the stabilised hydrazone cation, which can decompose in two ways. Under the conditions of Eastman and Detert[151], attack by acetate ion would lead to the highly delocalised product (28). This could then ring-close to form the substituted pyrazole (29, scheme 24). Under the anhydrous conditions existing in the decomposition of N-nitrosoacetnailide, the acetate ion will act as a much stronger base, and this could abstract a hydrogen from the hydrazone in either of the two ways shown in scheme 25 thereby opening the furan ring, and supplying the necessary precursor to the azo-substituted pyrazole.

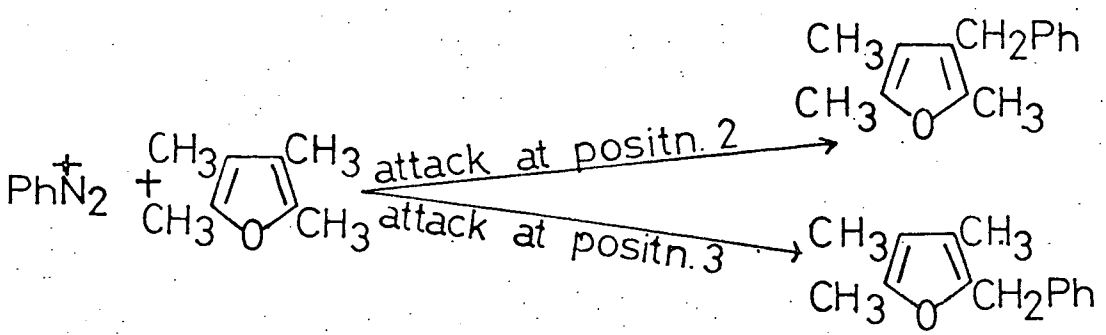
Stemming from this proposed mechanism for the formation of pyrazoles, a possible scheme can be proposed for the

formation of 2-benzyl-5-methylfuran which involves a common intermediate for the two reactions. The cation formed by the addition of the benzenediazonium cation to 2,5-dimethylfuran could either add acetate ion, and hence form the substituted pyrazole, or lose a proton from the 2--methyl group which could give 2-benzyl-5-methylfuran via a subsequent cyclic decomposition (scheme 26)



Scheme 26

As a test of the validity of this mechanism , N-nitrosoacetanilide was allowed to decompose in tetramethylfuran. In the case of tetramethylfuran, we can expect that the 2-position will be more reactive to electrophilic attack than the 3-position, drawing analogy to the case of furan. Thus, if the mechanism proposed in scheme 26 were operative, we could expect to obtain more of the 3-benzyl isomer, compared to the 2-benzyl isomer, in the decomposition of N-nitrosoacetanilide in tetramethylfuran.



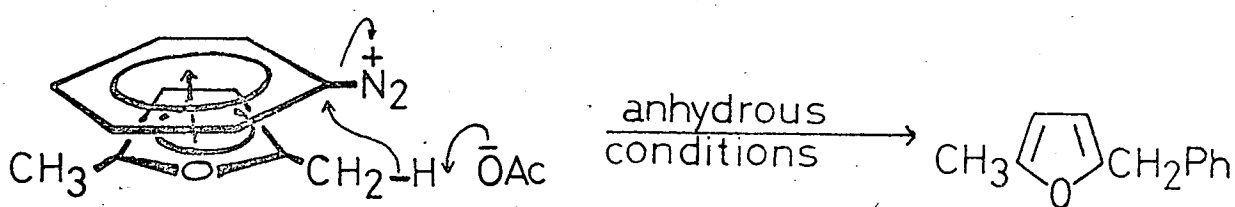
By comparison of the n.m.r. spectra of 2,5-dimethylfuran, tetramethylfuran, and furan, the methylene group of 3-benzyl-2,4,5-trimethylfuran was assumed to absorb at a higher τ value than that of 2-benzyl-3,4,5-trimethylfuran. The mixture of the two isomers obtained in the reaction was analysed by n.m.r. spectroscopy, and it was found that there was a preponderance of the 2-isomer over the 3-isomer. G.l.c. analysis gave the isomer ratio 2- : 3- = 8.6:1. This is in direct disagreement with the result which should have been obtained had the mechanism in scheme 26 been operative.

Had a common intermediate existed between the formation of substituted pyrazoles, and of 2-benzyl-5-methylfuran, it was reasoned that 2-benzyl-5-methylfuran should also be present in the reaction mixture from the decomposition of benzenediazonium chloride in 2,5-dimethylfuran by the method of Eastman and Detert[151]. None was detected, but the subsequent discovery that water had a strong repressant effect upon the yield of 2-benzyl-5-methylfuran in the decomposition of N-nitrosoacetanilide in 2,5-dimethylfuran invalidated the conclusions drawn from this observation.

The mechanism outlined in scheme 26 was considered to be improbable, not only from the results obtained from the decomposition of N-nitrosoacetanilide in tetramethylfuran, but also from the fact that the azo-group in the intermediate was required to have the cis- configuration and, moreover, scale models showed that overlap of the orbitals concerned

could only be achieved after the most tortuous contortions.

The results summarised in Table 9 show that 2-benzyl-5-methylfuran is only formed in those reactions known to involve the intermediacy of the benzenediazonium cation. Yoshida and Osawa[155] reported that 2,5-dimethylfuran was a stronger π-base than furan itself and so, in analogy to the case of furan, it might seem reasonable to postulate the formation of a π-complex between 2,5-dimethylfuran and the benzenediazonium cation. Formation of a π-complex of this sort would lead, not only to reduced acidity of the o-protons on the benzenediazonium cation, but also to increased acidity of the methyl protons on the furan nucleus. We can thus postulate that the acetate ion is basic enough under anhydrous conditions to remove one of the methyl protons. In solutions containing water, however, the base-strength of the acetate ion would be so reduced, that the abstraction of a proton from a methyl group would not be possible. The proposed mechanism is outlined in scheme 27.



Scheme 27

If the π-complex were involved, then substituents on the diazonium cation should affect the ease of formation of the complex, and hence the yield of the 2-arylmethyl-5-methylfuran. Inspection of Table 10 shows that no 2-arylmethyl-5-methylfurans are detected in the case of N-

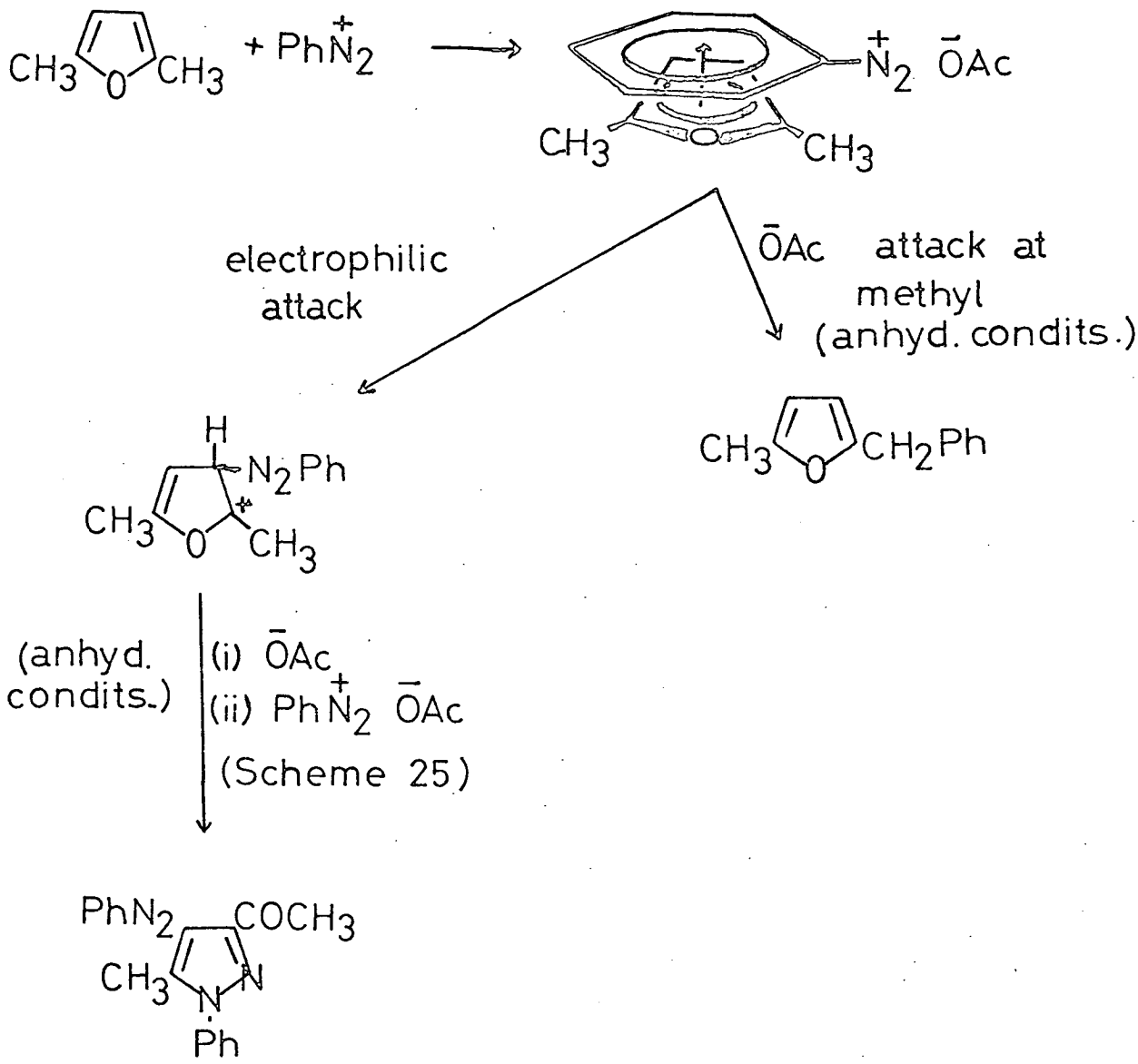
nitrosoacetanilides (and hence diazonium cations) which have electron releasing groups in the 4-position. Electron-releasing groups in the 4-positions should also weaken the π-complex by delocalising the positive charge. With the electron-withdrawing carbethoxy group in the 4-position of the nitrosamide, some 2-arylmethyl-5-methylfuran was isolated, albeit in smaller yield than in the case of N-nitrosoacetanilide itself, but in almost equal yield to that obtained from 3-carbethoxy-N-nitrosoacetanilide. The most interesting case presented in table 10 is that of 3-methoxy-N-nitrosoacetanilide, which gives a yield of 2-(3-methoxybenzyl)-5-methylfuran of 19 m/100m. The methoxyl group in the 4-position is electron releasing, whereas in the 3-position it is electron withdrawing. The methyl group is electron releasing in both positions and so, as could be predicted from this theory, the decomposition of 3-methyl-N-nitrosoacetanilide in 2,5-dimethylfuran gives a much smaller yield (9 m/100m) of the corresponding 2-arylmethyl-5-methylfuran.

It would be predicted that the decomposition of N-nitrosoacetanilide in tetramethylfuran, should give a higher yield of 2-benzyl-3,4,5-trimethylfuran than the yield of 2-benzyl-5-methylfuran obtained from the decomposition of N-nitrosoacetanilide in 2,5-dimethylfuran. This we would expect because of the higher electron density, and therefore the greater π-basicity, of the tetramethylfuran ring. The effect was only slight, however, the yields of 2-benzyl-3,4,5-trimethylfuran and of 2-benzyl-5-methylfuran being 28 m/100m and 27 m/100m respectively. In the converse case of 2,5-dimethyl-3,4-dicarbethoxyfuran, which should not form

a π-complex because of its low electron density, no compound could be detected to which could be assigned the structure of the corresponding substitution product. These results would suggest that π-complex formation is, indeed, an essential step in the formation of 2-benzyl-5-methylfuran in these reactions.

The formation of a π-complex as an integral part of the mechanism of the formation of 2-benzyl-5-methylfuran would also explain the sensitivity of the yield of 2-benzyl-5-methylfuran to temperature. Fission of the π-complex at elevated temperatures will lead, not only to lower yields of 2-benzyl-5-methylfuran (2.4 m/100m at 80°) but also to the formation of "normal" radical products, 5,5'-bifurfuryl (3.2 m/100m), and of the benzyne adduct 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene (0.04 m/100m). The fact that 4'-chloro-N-nitrosobenzanilide forms the benzyne adduct (1 m/100m) at room temperature can be explained by invoking the greater base strength of the 4-chlorobenzoyl anion, (and the extreme insolubility of 4-chlorobenzoic acid).

Thus, the o-protons of the diazonium cation can still be removed by the 4-chlorobenzoyloxy anion despite their acidity having been reduced, by π-complexing, to such an extent that the acetate anion is unable to remove them. This is in agreement with the observation of Brydon, Cadogan, Smith and Thomson[24], that higher yields of benzyne adducts were obtained from the decomposition of 4-chloro-N-nitrosobenzanilide over those obtained from the decompos-


+ PhN2
N2 OAc
CH3
CH3
electrophilic attack
OAc attack at methyl (anhyd. condits.)
CH2Ph
H
N2Ph
(anhyd. condits.)
(i) OAc
(ii) PhN2 OAc
(Scheme 25)
PhN2
COCH3
N
Ph

Scheme 28

ition of N-nitrosoacetanilide.

In conclusion, therefore, we can now postulate a mechanism for the formation of 2-benzyl-5-methylfuran in the decomposition of N-nitrosoacetnailide in 2,5-dimethyfuran. This mechanism invokes the formation of a π-complex between the benzenediazonium cation in solution and 2,5-dimethylfuran. The mechanism successfully explains the effects of temperature, substituents on both reactants, and water, on the yields of 2-benzyl-5-methylfuran. In addition, the formation of substituted pyrazoles in the reaction has been explained (scheme 28).

3. DECOMPOSITION OF DIBENZOYL PEROXIDE IN SUBSTITUTED FURANS.

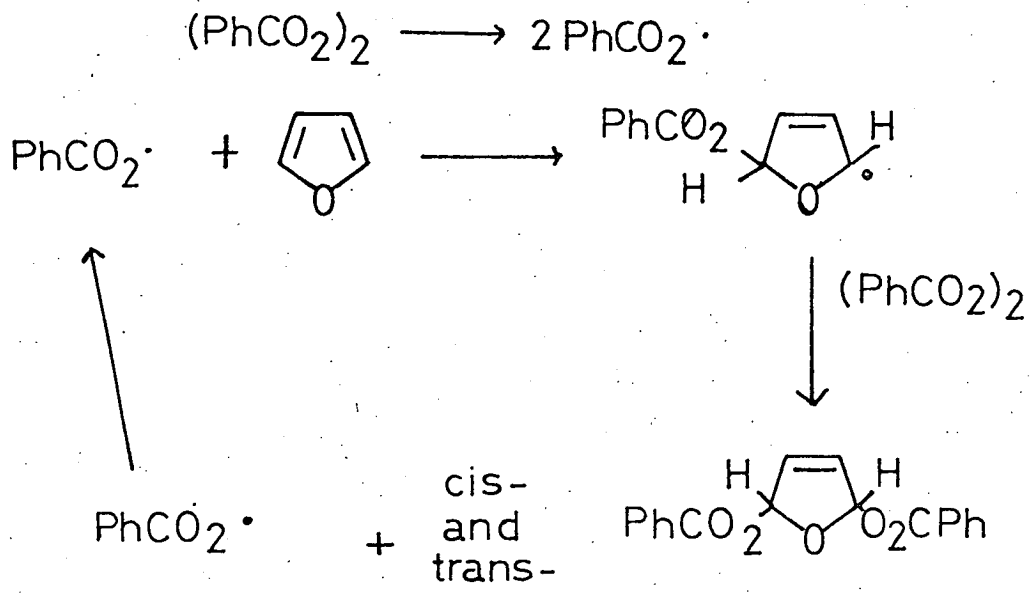
Dibenzoyl peroxide is known to decompose via two stages,[62,63] homolytic fission to form two benzoyloxy radicals

$$(PhCO_2)_2 \longrightarrow 2PhCO_2\cdot$$

which can be followed by fragmentation of the benzoyloxy radical, forming a phenyl radical and carbon dioxide.

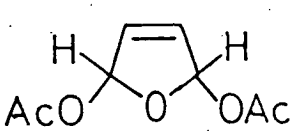
$$PhCO_2\cdot \longrightarrow Ph\cdot + CO_2$$

Kolbé and Black[159] reported that the decomposition of dibenzoyl peroxide in furan at 35° and 80° gave benzoic acid, and cis- and trans- 2,5-dibenzoyloxy-2,5-dihydrofuran with an accountancy of over 90%. Little carbon dioxide was detected, which would suggest a mechanism of the type outlined in scheme 29. Induced decomposition of the dibenzoyl peroxide would explain the high accountancy of peroxide in the reaction.



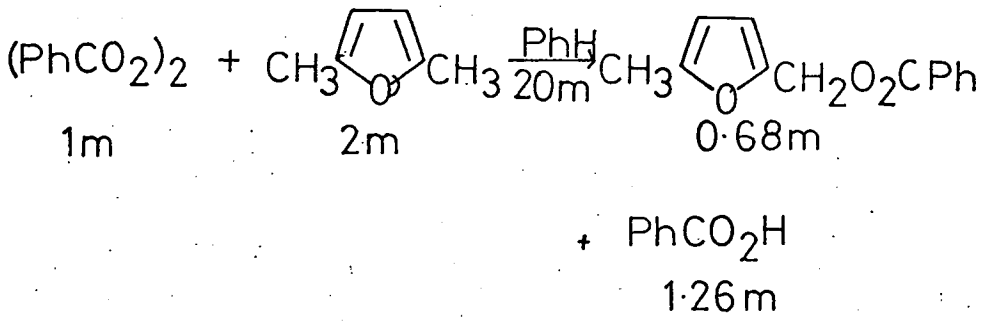
Scheme 29

Kolbé and Black also noticed that the reaction had an induction period at 35° of 7-14 days with freshly-distilled furan, but that the reaction was initiated much sooner with furan that had been allowed to stand in contact with the air, and develope peroxides. This evidence was taken to confirm the free radical nature of the reaction. Kolbé likened the reaction to one which he had reported earlier[160], in which the product from the electrolysis of a mixture of furan, sodium acetate, and acetic acid was found to be 2,5-diacetoxy-2,5-dihydrofuran (30).

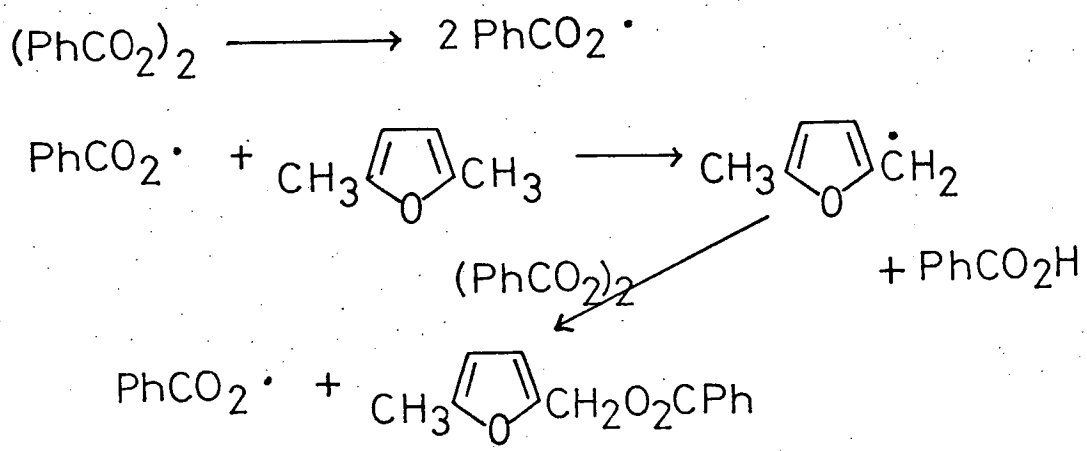


(30)

The decomposition of dibenzoyl peroxide in 2,5-dimethylfuran was found, in this investigation, to give 2-benzoyloxymethyl-5-methylfuran, and benzoic acid, with a high accountancy of 97%.



The suggested mechanism for this reaction is outlined in scheme 30.



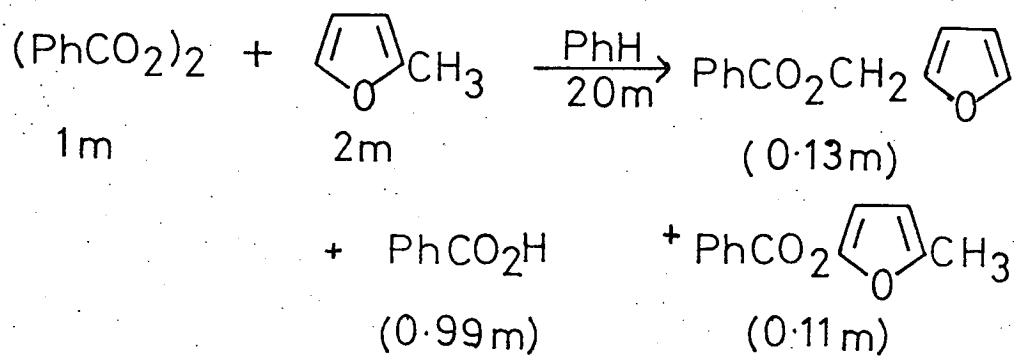
Scheme 30

Abstraction of a hydrogen from the methyl group by a benzoyloxy radical gives the 5-methylfurfuryl radical, which in turn, by induced decomposition of the dibenzoyl peroxide, gives the chain carrying benzoyloxy radical plus the product.

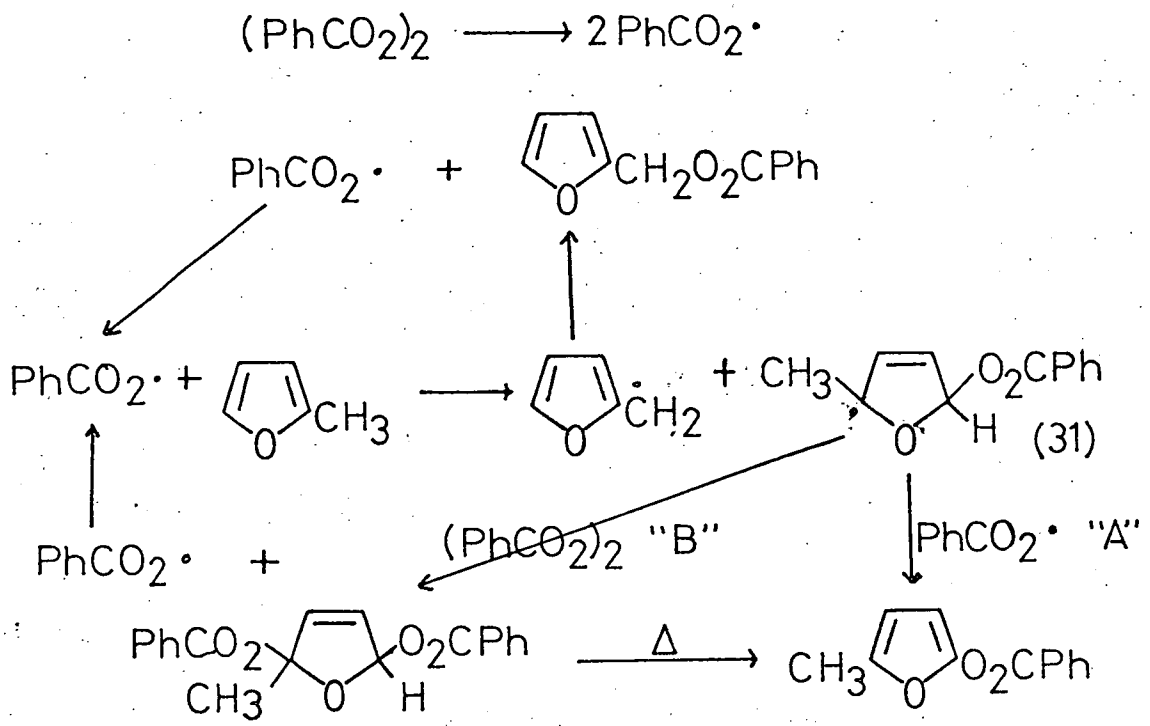
The fact that c.i.d.n.p. was not detected for this reaction does not constitute proof that the reaction follows

a non-radical pathway (although, the converse can be taken as conclusive proof of radical intermediacy in a reaction). The failure to detect c.i.d.n.p.' can be taken merely to suggest that the 5-methylfurfuryl radical has a shorter time of relaxation that its average lifetime in the presence of dibenzoyl peroxide.

The decomposition of dibenzoyl peroxide in 2-methylfuran was found to give 2-benzoyloxy-5-methylfuran, 2-benzoyloxymethylfuran, and benzoic acid.



The mechanism for this reaction is taken to follow the pathways illustrated in schemes 29 and 30 (scheme 31).



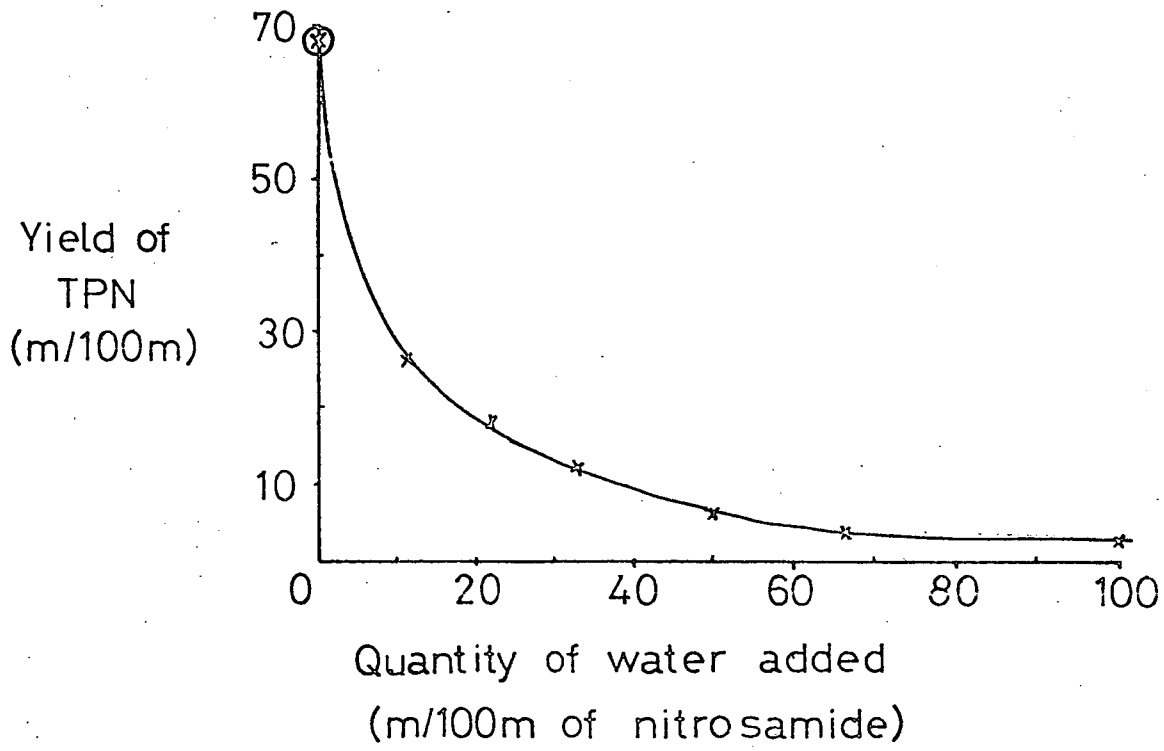
Scheme 31

The formation of 2-benzoyloxy-5-methylfuran can be explained by proposing two routes. The direct addition to the furan by a benzoyloxy radical can be followed, either by oxidation of the 2-benzoyloxy-5-methyl-2,5-dihydrofuryl radical (31) by a benzoyloxy radical (A) or, induced decomposition of dibenzoyl peroxide by 31 to form 2,5-dibenzoyloxy 2-methyl-2,5-dihydrofuran which decomposes to give 2-benzoyloxy-5-methylfuran and benzoic acid (B).

4 REACTIONS OF ARYLAMINES AND ORGANIC NITRITES : A NEW ROUTE TO ARYNES.

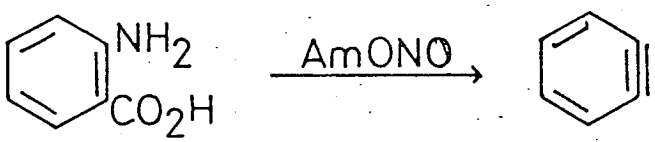
Attempts to find a simple route to arynes from

GRAPH II : The Effect of Water on the Yield of TPN from N-Nitrosoacetanilide/Tefracyclone



⊗ This result was obtained by Mr. A. Robertson

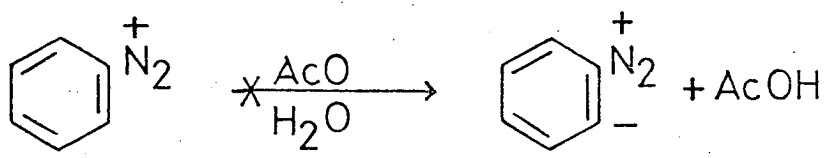
arylamines have long been made with varying success. Friedman and Logullo[18] had the first major success in this quest when they successfully prepared benzyne, in high yield, from pentyl nitrite and anthranilic acid.



The preparation of derivatives of anthranilic acid is, however, a tedious, and often difficult process, which limits the variety of arynes obtainable by this method. Cadogan's[24] discovery that N-nitrosoacylarylamines gave aryne adducts when decomposed in the presence of aryne traps was again of vital importance, but the difficulties involved in the preparation of these compounds made the method rather limited. Ruchardt and Tan[161] successfully produced benzyne (40%) from benzenediazonium fluoroborate in the presence of potassium acetate and acetic acid, which represented the simplest route to arynes from arylamines prior to the work described herein.

Early work in these laboratories had shown that the generation of benzyne from N-nitrosoacetanilide was extremely sensitive to the presence of water in the reaction mixture. A more complete study of this effect was conducted to determine the shape of the sensitivity curve, shown in graph 2 opposite, and to ascertain if this sensitivity was also apparent in the generation of benzyne from benzene diazonium

fluoroborate by the method of Ruchardt and Tan[161]. This was found to be the case, the yield of TPN dropping from 30/m/100m in the absence of water to 3 m/100m in the presence of 100 m/100m of added water, when benzenediazonium fluoroborate was decomposed in this manner, using tetracyclone as the aryne trap. The sensitivity of these reactions to the presence of water can be attributed to the fact that the basicity of the acetate anion will be greatly reduced in the presence of a compound capable of forming hydrogen bonds. Hydrogen bonds will form with the anion so reducing the basicity of the anion to such an extent, that removal of the o-proton in the benzenediazonium cation is no longer possible.



Amyl alcohol, which can also form hydrogen bonds, was found to have a similar effect.

Cadogan[75] had previously reported a new method of aromatic substitution, based upon the generation of phenyl radicals by the in situ diazotisation of aniline by pentyl nitrite. The reaction was thought to proceed via diazonium cation, but, since water was produced as a by-product, the formation of a benzyne/benzynoid intermediate would be suppressed. Several attempts by earlier workers in these laboratories to produce benzyne from aniline and pentyl nitrite had been unsuccessful despite their adding

dehydrating agents of various types to the system.

It was decided to continue this line of research employing acetic anhydride in the dual rôle of a dehydrating agent and a source of acetate ions. Consequently, pentyl nitrite, potassium acetate, acetic acid, acetic anhydride, aniline, and tetracyclone were boiled together,and TPN was isolated from the reaction mixture in 15% yield. A similar experiment using 2,5-di(4-methylphenyl)-3,4-diphenylcyclopentadienone as the aryne trap gave 1,4-di(4-methylphenyl)-2,3-diphenylnaphthalene in 15% yield. A successful attempt to increase the yield of TPN obtained in this reaction was tackled, by varying the parameters of the reaction conditions. This is summarised in Tables 4 and 3 pp73 and 74). Once the optimum reaction conditions had been found, the yield of TPN from tetracyclone had been raised to 32% and the yield of triptycene from anthracene was found to be 10%. A selection of other dehydrating agents was also applied to the reaction, the yields of adduct being given in Table 11.

Table 11 : The use of a Series of Dehydrating Agents in the Reaction of Pentyl Nitrite/Aniline.

Dehydrating Agent	Yield of TPN (m/100m)
Acetic Anhydride	32
Acetyl Chloride	20
4-chlorobenzoic Anhydride	39
Phosphorus Pentoxide	0

The greater basicity of the 4-chlorobenzoyloxy anion[24],

which leads to the more efficient removal of the o-proton from the benzenediazonium cation, is apparent when 4-chlorobenzoic anhydride was used as the dehydrating agent/anion source. In this case the yield of TPN rose to 39 m/100m. As was expected, phosphorus pentoxide gave no adduct, and the use of acetyl chloride in the reaction gave the adduct, although not in such high yields as those obtained from the use of acetic anhydride. The polarity of solvents was found to affect the yield of adduct only to a small extent, the results of the investigation being given in Table 12.

Table 12 : The Effect of Solvent Polarity on the Yield of TPN from Aniline/Pentyl Nitrite/Acetic Anhydride.

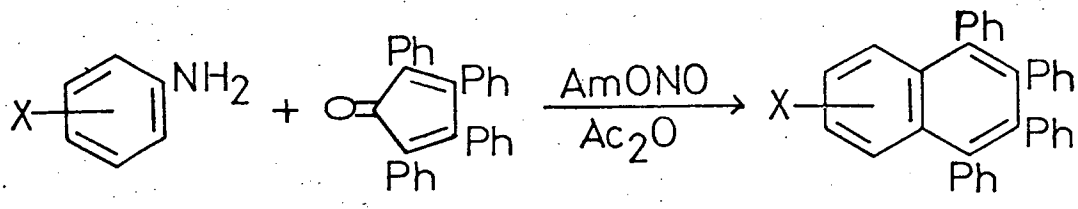
Solvent Used	Yield of TPN (m/100m)
1,2-Dimethoxyethane	20
Cyclohexane	17
Benzene	27

The results obtained from an investigation using a series of arylamines are given in Table 13.

A more comprehensive study of substituent effects in this reaction is reported and discussed elsewhere[162].

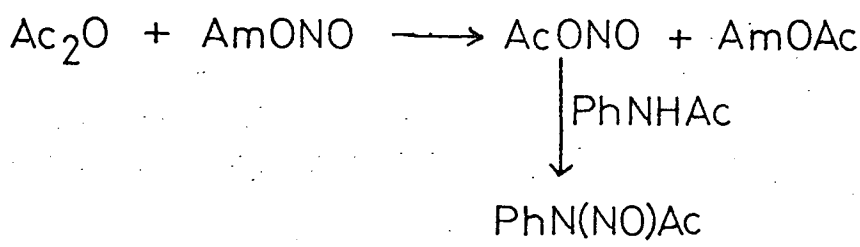
The optimum conditions for the formation TPN from pentyl/nitrite/acetic anhydride/aniline, the addition of pentyl nitrite to a boiling mixture of the other reactants in benzene, suggested that the use of acetanilide in place of aniline in the reaction mixture should give a similar result as, by the time that the pentyl nitrite was added, little aniline would remain.

Table 13 : The Use of Other Arylamines in the Reaction of Pentyl Nitrite/Arylamine/Acetic Anhydride.



		Yield m/100m
X = 3Cl	X = 5-Cl	18
3Br	5-Br	21
3-OMe	5- and 6-OMe	29
3-Me	5- and 6-Me	25.5
4-Me	6-Me	4.0
H	H	32

Thus the reaction of acetanilide/acetic anhydride/pentyl nitrite gave 21% of TPN. Since the reaction of pentyl nitrite and acetanilide produces no water, it was reasoned that there would be no necessity for the presence of acetic anhydride in the reaction mixture. It was found, however, that in the absence of acetic anhydride, the yield of TPN from acetanilide dropped to 7%, implying that acetic anhydride has some other function in the reaction save that of supplying acetate ions and acting as a dehydrating agent. The most likely rôle of acetic anhydride, outwith those mentioned, is that of reacting with pentyl nitrite to form transient acetyl nitrite, which is nitrosating acetanilide to form N-nitrosoacetanilide. The N-nitrosoacetanilide will then decompose in its normal manner for form benzyne.



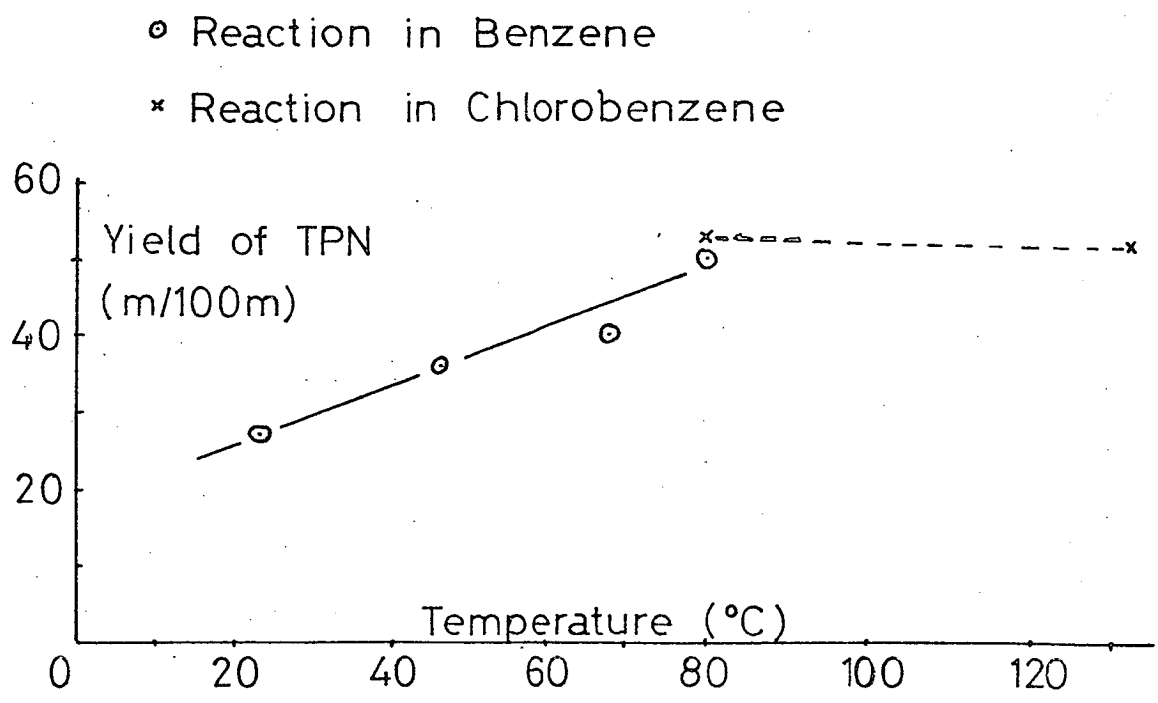
Bearing this mechanism in mind, and the extreme instability of acetyl nitrite, a more stable nitrite which might possess better nitrosating properties was sought. Benzoyl nitrite was considered a substitute, as it has a good leaving group in the benzoyloxy group, and is fairly stable. This was superceded by the use of 4-chlorobenzoyl nitrite, which possesses an even better leaving group. The results obtained from experiments involving these nitrites are summarised in Table 14.

Table 14 : The Use of Aroyl Nitrites as Nitrosating Agents.

Reactants Used.	Yield of TPN obtained
Benzoyl Nitrite/Aniline	9.0
4-Cl C_6H_4 $CO_2NO/PhNH_2/Ac_2O$	38.0
4-Cl C_6H_4 $CO_2NO/PhNH_2/(4\text{-Cl } C_6H_4 \text{ } CO)_2O$	45.0
4-Cl $C_6H_4CO_2NO/PhNH \cdot CO \cdot C_6H_4 \cdot$ 4-Cl	48.0
4-Cl C_6H_4 $CO_2NO/PhNHAc$	51.0

The use of benzoyl nitrite in the triple rôle of benzoylating agent, dehydrating agent, and nitrosating agent proved rather unsuccessful, but was followed by the successful use of 4-chlorobenzoyl nitrite/acetic anhydride/

GRAPH I : The Effect of Temperature on the yield of TPN, from 4-Chlorobenzoyl Nitrite/ acetanilide/Tetracyclone



aniline giving TPN in 38% yield. It was reasoned that, in this reaction, the 4-chlorobenzoyl nitrite might be exchanging with acetic anhydride forming acetyl nitrite, thus making the yield of TPN approach that obtained in the case of pentyl nitrite/acetic anhydride/aniline. Acting on this premise, 4-chlorobenzoyl nitrite was employed in the rôle of of nitrosating agent and, if necessary, dehydrating agent, in its reaction with acetanilide. The yield of TPN was much improved, and was not bettered, even by the systems 4-chlorobenzoyl nitrite/aniline/4-chlorobenzoic anhydride and 4-chlorobenzoyl nitrite/4^1-chlorobenzanilide. This was a little disappointing, as it had been expected that the superior removal of the benzenediazonium cation o-proton by the 4-chlorobenzoyl anion might lead to larger yields of TPN as had been the case of pentyl nitrite/aniline/4-chlorobenzoic anhydride, and 4^1-chloro-N-nitrosbenzanilide. Similarly, the presence of sodium 4-chlorobenzoate in the reaction mixture led to a decrease in the yield of TPN.

An investigation of the effect of temperature on the reaction 4-chlorobenzoyl nitrite/acetanilide/tetracyclone indicated an optimum reaction temperature of 80°, the yield of TPN at this temperature being approximately 55%. The results of the investigation are presented in Graph 1.

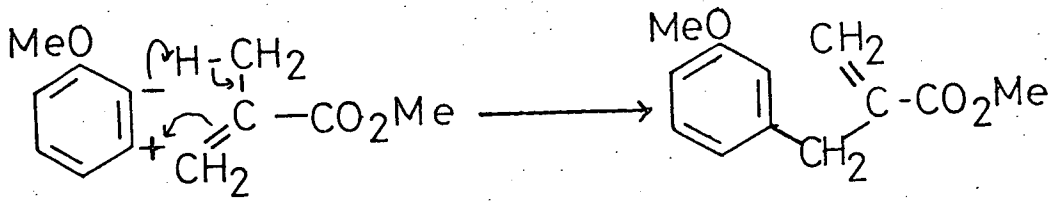
In a further attempt to increase the yield of TPN from 4-chlorobenzoyl nitrite/acetanilide/tetracyclone, high dilution experiments were conducted in the hope that the radical redox reaction might be curtailed in favour of benzene formation when the concentration of benzenediazonium

cation was lower. The yield of TPN from these reactions was successfully raised to 70%, and, under these conditions, various other aryne traps were used in the reaction. The results of these experiments are summarised in Table, 15.

Table 15 : High Dilution Reaction of 4-Chlorobenzoyl Nitrite/ Acetanilide/ Aryne Trap.

Aryne Trap Employed	Yield of Adduct (m/100m)
Tetracyclone	70
Anthracene	16
9,10-Dimethoxyanthracene	14
Methyl Methacrylate	31

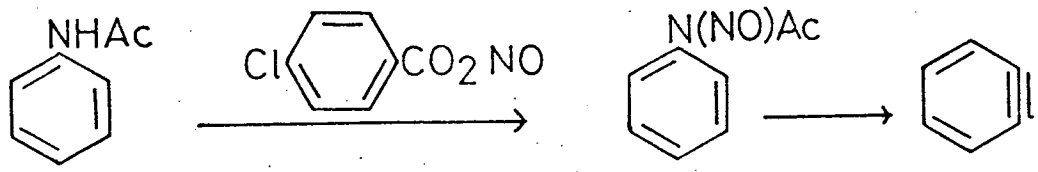
Cook[117] reported that when N-nitrosoacetanilide was decomposed in the presence of 9,10-dimethoxyanthracene, the yield of 9,10-dimethoxytriptycene was 15%. The corresponding yield of triptycene from anthracene was 5%. The reaction of methyl methacrylate with benzyne was reported by Tabushi[163], and belongs to the class of "ene" reactions. This reaction was found to be stereospecific in the case of 3-methoxybenzyne, since the decomposition of 4-chlorobenzoyl nitrite/3-acetaniside gave 2-carbomethoxy-3-(3-methoxyphenyl)prop-1-ene (25%). N.m.r. spectroscopic analysis would have detected 5% of the 4-methoxyphenyl isomer. The stereospecificity of the reaction can be explained in terms of the polarity of the reacting species.



Klandermand and Criswell[28,29] reported the greater reactivity of 9,10-demethoxyanthracene towards benzyne over that of anthracene. They obtained a rate ratio for the attack on these two traps by benzyne of K_H^{oMe} = 2.7, whereas Cook[117] obtained a value of 3.2 from the decomposition of N-nitrosoacetanilide and from pentyl nitrite/anthranilic acid. A competitive experiment involving these two traps and 4-chlorobenzoyl nitrite/acetanilide gave a rate ratio K_H^{oMe}=2.85, which lies within the observed range of the rate ratio observed for benzyne. Klanderman and Criswell[28.29] have also reported that, in the reaction of benzyne with 1,4-dimethoxyanthracene, the ratio of "B" ring adduct to "A" ring adduct formed is independant of the benzyne source, having a value K_A^B = 2.1-2.6 except in the case of diphenyliodonium -2-carboxylate, where the ratio K_A^B was 3.5. The reaction of 4-chlorobenzoyl nitrite/acetanilide with 1,4-dimethoxyanthracene gave a rate ratio of K_A^B = 3.2, which is a little higher than the value predicted by Klanderman and Criswell.

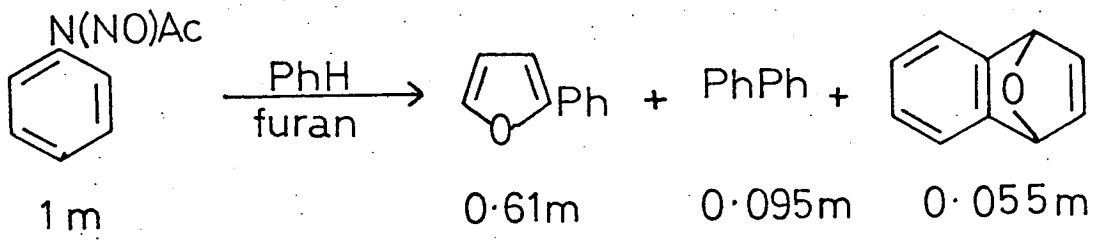
The mechanism of the reaction of 4-chlorobenzoyl nitrite and acetanilide in the presence of benzyne traps can be postulated to involve an initial nitrosation of acetanilide to form N-nitrosoacetanilide, which decomposes

to benzyne via its usual route.

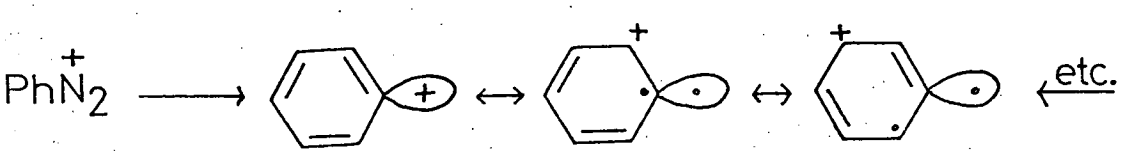


This postulated mechanism has been supported by Robertson[162], who has conducted a survey of substituent effects, and kinetics of this reaction, and the reaction of pentyl nitrite/acetic anhydride/aniline, which is suggested to follow a similar route via transient formation of acetyl nitrite. In addition to the case of decompositions in the presence of methoxy-substituted anthracenes, a further discrepancy occurs between the decomposition of N-nitrosoacetanilide and of 4-chlorobenzoyl nitrite/acetanilide. In competition experiments including furan and benzene with these two sources of benzyne, N-nitrosoacetanilide gives a rate ratio of $K^{furan}_{benzene} = 15.9$; whereas 4-chlorobenzoyl nitrite/acetanilide gives a rate ratio of $K^{furan}_{benzene} = 9.0$. The authentic radical source pentyl nitrite/aniline gives a rate ratio of $K^{furan}_{benzene} = 4.8$. The decomposition of N-nitrosoacetanilide had been conducted at room temperature, while the remaining two reactions had been conducted at the boiling point. Unfortunately the rate ratio is not available for the high-temperature decomposition of N-nitrosoacetanilide. Figures are available, however, for the high temperature decomposition of N-nitrosoacetanilide in a boiling mixture of not quite equimolar furan/benzene,

which had been conducted for other reasons, which show that, at the higher temperature, the rate ratio drops to $K^{furan}_{benzene} \approx 6.5$.



This would suggest that, as the temperature increases, the rate of phenylation of furan and benzene changes relative to each other, the rates becoming more equal as the temperature is increased as we would expect. The anomalous result obtained in the case of the decomposition of benzenediazonium fluoroborate/acetic acid/potassium acetate, at 57°, of $K^{furan}_{benzene} = 16.5$ (Table 7), can be accounted for by proposing the intermediacy of an electrophilic radical ion, similar to that of Abramovitch[73]. This electrophilic



species would show a marked preference for the furan nucleus over benzene.

To summarise, we can say that the simplest route to arynes from arylamines yet reported has been developed, the decomposition of pentyl nitrite/aniline/acetic anhydride producing TPN in 32% yield from tetracyclone.

A development of this reaction, the decomposition of 4-chlorobenzoyl nitrite/acetanilide, has produced TPN in 70% yield from tetracyclone. Both of these reactions are believed to proceed via nitrosation of the acylarylamines, forming the N-nitrosoacylarylamine, which decomposes by its established route to benzyne.

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